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Drug and Cosmetic Industry

Contents

February 1961 Vol. 88 No. 2

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Drug & Cosmetic Industry is published monthly by Drug Markets, Inc. Frazer V. Sinclair, President and Treasurer; Paul Alexander, Executive Vice-president and Secretary. Editorial and General Office: 101 West 31st St., New York 1, N. Y., U.S.A. Telephone, LOngacre 3-3177. Publication Address: Sun Printing Corp., 28 Renne Ave., Pittsfield, Mass., U. S. A.

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Midwestern Advertising Representative: Dwight Early and Sons, 100 No. LaSalle St., Chicago 2, Telephone, CEntral 6-2184. West Coast Advertising Representative: Dillenbeck-Galavan, Inc., 266 S. Alexandria Ave., Los Angeles 4, Telephone, DU 5-3991.

Subscription price $3.00 a year, in advance. Foreign Countries, $5.00. Single copies, 35c. Back issues 50c. Second-class postage paid at Pittsfield, Mass. Member of Audit Bureau of Circulation.

Copyright 1961
by Drug Markets, Inc., Vol. 88, No. 2.

By the publishers of ***Drug and Cosmetic Industry***

Beauty Fashion. The magazine of personal selling. Yearly subscription in the U.S.A., $3.00.

Drug and Cosmetic Catalog. Directory and data for manufacturers. Published every two years. $4.00 in the U.S.A.

Trade Mark Record and Supplements. Complete trade-mark listing of perfumes and cosmetics. $15.00.

Books. Technical information for manufacturers of drugs and cosmetics.

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I don't think we need any further research for perfuming this product. My wife likes this odor.

Keeping Posted

Aspirin for Income Taxers

The Iowa Executive Council rejected a request by tax commission employees in Des Moines that they be provided with free aspirin during the approaching income tax season. Alert PR people at Plough discovered the plight of the Des Moines tax checkers and sent them a complimentary supply of St. Joseph Aspirin. The aspirin was forwarded with best wishes for a joyous, clear-headed income tax season.

Pre-Testing Cosmetics

Representative Sullivan has introduced a bill amending the Food, Drug, and Cosmetic Act which contains a section relating to the pre-testing of cosmetics. Further, with respect to cosmetics, the bill would provide for testing for carcinogenicity. Three important provisions call for elimination of soap exemption so that soaps would be covered by the Act; hair dyes, even when properly labelled would not be exempt from the operation of the Act; all cosmetics would have to contain in their labelling the name of each ingredient used in the cosmetic. S. L. Mayham, executive vice-president of the Toilet Goods Association, points out that the pre-testing provision does not provide for exempting products that may have been on the market for many years and it might entail testing of over 100,000 products now being marketed. The bill has apparently been drafted for the legislative mill without adequate attention to practicability and the serving of the best interests of both consumers and manufacturers.

Trademark Activity 1960

Trademarks increased their importance in the industrial picture in 1960 as illustrated by a record number of registrations issued during the year and reported by the United States Trademark Association in its annual review of trademark activities on an international, Federal, state, and corporation level. A total of 18,436 trademark registrations were issued for the second largest number in any one year, topping 1959 by 116. Some 22,802 applications for trademarks were filed with the U. S. Patent Office, 162 fewer than in 1959.

Among new trademarks, Brand X proved popular during the year and applications were filed to register the designation for cigarettes, cleaning compound and polishing cloth, and popcorn.

There was little activity with respect to legislation during 1960; a number of bills affecting trademarks were introduced in Congress, but no action was taken and they died with adjournment.

The U. S. Trademark Association lodged informal protests in 1960 through diplomatic channels against applications to register 77 generic words as trademarks in more than 11 countries.

The courts indicated an unwillingness to condone some "commercial hitchhiking." The beer slogan "Where there's life . . . there's Bud" received judicial protection through injunctive relief in two actions brought against companies which were using "Where there's Life . . . there's Bugs" for a floor wax containing an insecticide.

Action against counterfeiting popular drug trademarks took place when the State of New Jersey apprehended counterfeiters who were reported to have netted about $50,000 a month for two years. Trademarks being counterfeited were those owned by Ciba, Schering, Warner-Chilcott, Wallace, Merck, SK&F, and Wyeth.

The imitation of drug products received a judicial setback in an action brought by Smith Kline & French against a defendant who duplicated exactly the distinctive appearance of certain of its popular items. In marketing the imitations, the defendant specifically named the produce of the plaintiff which it duplicated, called druggists' attention to the identical appearance, and, in one instance, did no more than mail a sample of one tablet without even identifying its formulation. The defendant's prices were only a fraction of that of the plaintiff, which en-

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couraged substitution by druggists. The court ordered the defendant to discontinue these unfair acts and awarded the plaintiff damages of $6,250.

The mark DU BARRY, long used for a line of cosmetics, was found to be infringed by another's use of the same mark for scarves, bags, aprons, brushes, hairnets, roller pins, beauty caps, complexion cloths and similar items and the defendant compounded the confusion by using the terms "Famous," "Original," "Genuine" with the mark DU BARRY and, additionally, using a script style and crown design similar to that of the plaintiff.

Reversing the ruling of the trial judge, a federal appellate court in New York found that the mark VALCREAM infringed upon BRYLCREAM, both being used for men's cream hair dressings. Influencing the upper court were the similarities between the products, their tube size, prices, packaging designs and colorations and the fact that the defendant's package designer had the BRYLCREAM tube before him when he started to work. In concluding that the defendant should discontinue the mark VALCREAM, the court was also influenced by the confusion evident in a promotional offer of the defendant which required purchasers to send in a VALCREAM carton. Thirteen persons sent in BRYLCREAM cartons to the plaintiff in response to the defendant's offer.

Medical Advertising Costs

A study conducted by Cortez F. Enloe, Inc., medical advertising agency, shows that average medical journal space costs have risen about 60 per cent since 1950, while direct mail costs in the same period have increased by 33 per cent, and bulk postage rates by 150 per cent. In the same time, the average medical practitioner is being exposed to more than four times the number of medical journal advertisements. In 1960, a drug advertiser had to spend $4.50 to achieve the same advertising exposure that cost $1 ten years ago.

Cardiovascular Preparations Market

According to a study made by the market research department of MODERN MEDICINE, the total cost to the patient for treating cardiovascular disease is about $592,000,000 annually, divided among physicians' fees of $171,000,000, hospital and other care $135,000,000, and drug cost $286,000,000. Of ten million persons with cardiovascular disease, about seven million are under medical care, and these are about equally divided between those with high blood pressure and those suffering from heart conditions. At the manufacturers' price level—average discounts of 50 and 15 per cent of the price to the patient—preparations for treating high blood pressure were valued at about $90,000,000 and those for cardiovascular conditions at $32,000,000. The latter group includes digitalis preparations valued at $8.5 million, xanthines at $5.7 million, and others totaling $17.7 million. Products for treating high blood pressure include rauwolfias valued at $23.6 million, other hypotensives $19.2 million, diuretics as hypotensives $29.6 million, coronary vasodilators $13.8 million, peripheral vasodilators $3.8 million.

Increases in the drug treatment of hypertension stem from a change in medical thinking, from passive and conservative treatment to an active and vigorous attack. There is recognition that even "benign" hypertension will ultimately cause death directly or indirectly; reduction of hypertension by surgical means definitely increases life expectancy; potent drugs and procedures for treatment are now available.

Foreign Drug Purchases

The Military Medical Supply Agency announced three new contracts totaling $868,000 to foreign drug manufacturers—Farmochimica Cutolo-Calosi of Naples, Societa Zambon of Vincenza, Italy, and A-S Syntetic of Grindsted, Denmark. Although a Presidential order limits military purchases abroad, MMSA foreign purchases have been within the limits imposed by the order and purchasing officers are still required to seek lower drug prices abroad whenever domestic drug prices are considered to be unreasonably high.

Water Taste and Odor

A research project to determine adequate standards for testing taste and odor in our public water supplies is now being carried out at the Franklin Institute, Philadelphia, under the sponsorship of the Manufacturing Chemists' Association. The project will attack the highly complex problems of what is a "bad" taste or odor, and how it can be measured.

This phase of the program will look at various aspects of the taste and odor problem: chemical, biological, psychological, and physiological. A special air-conditioned panel testing laboratory for the experimental work is nearing completion. Here the Franklin Institute investigators will attempt to pin down some of the subjective aspects of taste and odor. Panels composed of persons of various ages, smoking habits, and medical histories will be used to determine the effect of various types and intensities of odors, time relationships, and complicated interactions among these factors.

The first aim will be to find some reproducible method for measuring the intensity of an odor. Later, Institute investigators will attempt to create a system for characterizing or labelling odors, so that all scientists working in the field will have common terms of reference.

American Foundation for Pharmaceutical Education

Charles D. Doerr, McKesson & Robbins, Inc., was elected president of the American Foundation for Pharmaceutical Education at the 19th annual meeting. George F. Smith, former president of Johnson &

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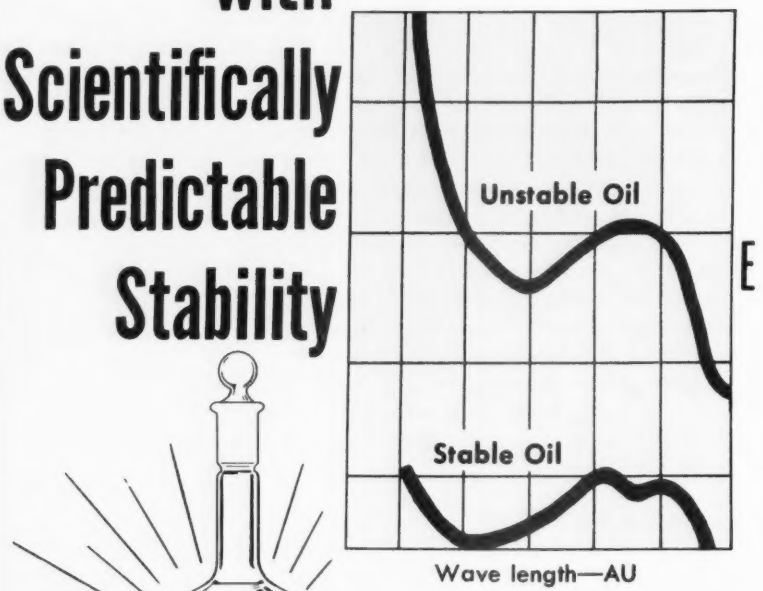

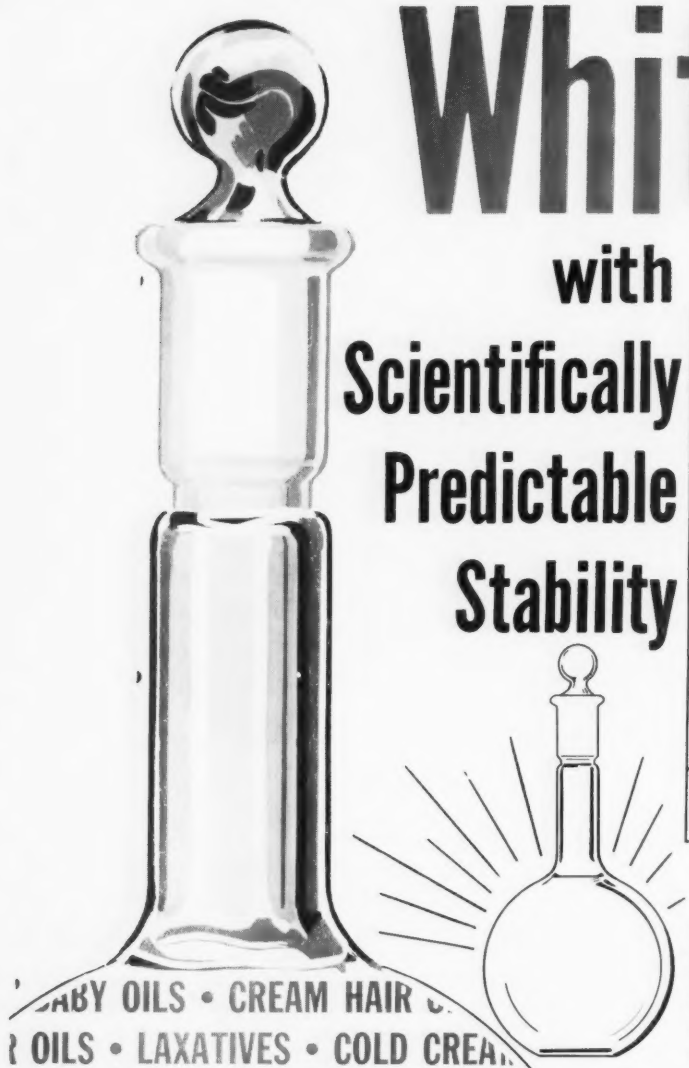

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• CLEANSING CREAMS • BEAUTY LOTIONS
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Johnson was elected vice-president; Carl K. Raiser, Smith Kline & French, was re-elected treasurer; James F. Hoge was re-elected counsel; W. Paul Briggs was re-elected secretary.

A budget of $265,000 was approved in support of educational products for 1961-1962. More than half of this budget is allocated to graduate fellowships; $25,000 goes for undergraduate scholarships and the Foundation supports the American Council on Pharmaceutical Education, annual pharmacy teachers' seminars, "The American Journal of Pharmaceutical Education," and pharmacy student recruitment programs.

Chloramphenicol Approved Again

George P. Larrick, Commissioner of Foods and Drugs, has announced that a panel of distinguished physicians appointed by the National Research Council at FDA's request has found that the antibiotic chloramphenicol is a valuable drug that should remain on the market for use in treating serious infections under medical supervision both in hospitals and for treatment of patients in the home. The panel also recommended revision of the labeling of the drug to give added emphasis to the warnings against its use in minor infections and calling attention to the necessity for adequate blood studies when use is required.

It was also the consensus of the NRC panel that: "The information should be disseminated as a warning on the drug label and elaborated in an enclosure in the drug package. Beyond this, there is need for continuing education of the physician through the media of medical meetings and the medical literature. This, of course, is a responsibility of the leaders of medicine and not of the Food and Drug Administration.

"More effective education of physicians in the proper use of drugs must be a continuing consideration. The role of the pharmaceutical companies in post-graduate medical education cannot be overestimated. Leaders in medicine must face this situation boldly and realistically if standards of practice are to be improved. The medical educators who constitute the editorial boards of a number of medical journals could exert some influence if they would improve the advertising that appears in their journals."

Essential Oil Prices

In his report at the 30th annual meeting of the Essential Oil Association of the U. S. A., R. E. Horsey, association president and vice-president of Givaudan-Delawanna, noted that most essential oil prices remained steady during the past year, with the exception of citronella, lemongrass, and sandalwood. The strong market in these oils has given greater impetus to the production of synthetics, which may eventually make the industry independent of natural products. Geranium Reunion oil rose to a high because of cyclone damage, while the effect of government rulings on safrol have not yet been reflected in the price of Ocotea Cymbarum. Present indications for 1961 are for steady and strengthened prices, without overproduction in relation to consumption.

External Red D&C No. 15

FD&C Red No. 1, decertified because preliminary tests showed that it caused liver damage when fed to test animals, has now been reinstated as permissable for external use only. This action is in response to petitions by the TGA others for the provisional relisting of the color, which will now be designated as External Red D&C No. 15.

Oral Polio Vaccine

In a letter apearing in the January 14 issue of the *Journal of the American Medical Association*, Dr. Hilary Koprowski, who developed a live polio vaccine bearing his name, challenged the statistical and scientific basis of the U. S. Surgeon General's decision last August to withhold approval of Koprowski's polio strain for vaccine production in the United States. Dr. Koprowski maintained that the safety of his preparation had been proven in one of the largest clinical trials in the history of science. The vaccine is reported to have been given to more than nine million people with no ill effects. The Surgeon General based his decision on tests in 131 monkeys performed by the U. S. Public Health Service Division of Biologic Standards, but Dr. Koprowski contends that his attenuated strain was developed to be used in man and not in monkeys. He further contends that the statistical differences shown were not significant.

In the final paragraph of his letter, Dr. Koprowski says, "Although it is a step forward that the principle of live virus immunization in poliomyelitis has at last been officially accepted, I am taking strong exception to this exclusive endorsement of one set of strains. In my opinion, such an endorsement should evoke a protest from individuals who believe that fair scientific judgment should be the basis for decisions affecting the physical welfare of man."

Dr. Sabin's almost inevitable response should be worth reading.

Shulton Promotional Allowances

An order by a Federal Trade Commission hearing examiner would require Shulton, Inc., to stop making discriminatory promotional payments to favored customers. This is not a final decision of the Commission and may be appealed, stayed, or docketed for review.

Examiner Walter R. Johnson found that Shulton has paid allowances to some customers for advertising or other services but did not make them available to all other competing customers. This discrimination,

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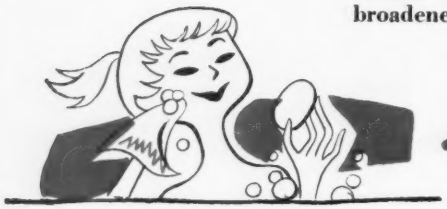

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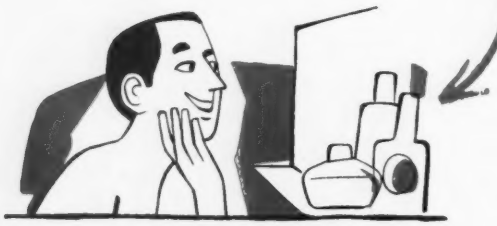

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Deodorant Colognes
Deodorant Powder
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Baby Powders
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he held, violates Section 2(d) of the Robinson-Patman Amendment of the Clayton Act. He pointed out that the concern had filed an answer admitting all material allegations in the FTC's complaint, waiving a hearing, but reserving its right to submit proposed findings of fact and conclusions of law and any other rights it may have under Commission rules.

Merck and Delagrange to Cooperate

Laboratoires Delagrange, French pharmaceutical company, and Merck Sharp & Dohme International. announced an agreement for joint chemical and pharmaceutical production in France. They have acquired joint ownership of the French chemical firm of Synorga S.A., which will be renamed Compagnie Chimique Merck Sharp & Dohme S.A., and are establishing a new jointly owned pharmaceutical company to be known as Merck Sharp & Dohme S.A.

Colgate Buys Wash-N'-Dri

Colgate Palmolive Co. has bought for $3 million in cash the consumer products division of Unexcelled Chemical Corp. The division makes Wash-N'-Dri pre-moistened towels and related products and the sale includes a manufacturing and packaging plant at Canaan, Conn. The Unexcelled consumer products division was R. R. Williams, Inc., until January 1960, when Unexcelled bought it for 103,682 shares of Unexcelled stock. Stockholders of Unexcelled will be asked to approve the sale of the division to Colgate.

Atlas Powder and Stuart Co. Intend to Merge

Ralph K. Gottshall, president of Atlas Powder Company and Arthur Hanisch, president of the Stuart Company, announced the signing of a memorandum of intent to merge the two companies. Stuart is an ethical pharmaceutical company with sales of $8,542,648 and net income of $1,101,371 for the year ended March 31, 1960, while Atlas Powder Company, making explosives and industrial chemicals, for the nine months ended September 30, 1960 had sales of $53,801,000 and net income of $2,638,000.

The merger involves a four-for-one split of Atlas common stock and shareowners of Stuart, except the principal holders who own 65 per cent of the common stock, will be offered one and one-half shares of the new Atlas common stock for each share of Stuart held. The three principal Stuart shareholders will receive one share of a new Atlas Class A stock for each five shares of Stuart held; each share of this class A stock can be converted at the rate of 20 per cent at the end of each year into six shares of the new Atlas common stock, which makes these holdings of each share of Stuart stock equivalent to 1.2 shares of new Atlas common stock.

The merger agreement will be submitted for approval to the boards of directors and stockholders of each company. Following approval, the Stuart Company will be operated as a division of Atlas, staffed and directed by Stuart management and personnel.

New Offerings

Softol, Inc., is offering, through Harwyn Securities, Inc., 150,000 shares of common stock at $2.00 per share. The company has outstanding 1,000 shares of $100 par value 5 per cent non-cumulated preferred stock convertible to 50,000 shares of common stock, and is authorized to issue 1,000,000 shares of common stock of which 500,000 shares have been issued and are outstanding. The company is engaged in the manufacture and sales of various cosmetic and toiletry items including Mascara Magic, Softol, Manicure Magic and aerosol fragrances. Sales in 1958 amounted to $83,769 with net loss of $20,611; in 1959 sales were $70,066 and net loss $11,232. For the first seven months of 1960 sales were $47,526 net profit, $114.

Cove Vitamin & Pharmaceutical, Inc., offers 108,000 units, consisting of 108,000 shares of common stock along with 108,000 shares of common stock purchase warrants, for $3.125 per unit, through Hill, Thompson & Co., Inc., and Globus, Inc. The company was organized on September 24, 1959 to engage in the mail order marketing of vitamins through department stores. Sales from September 24, 1959, were $15,751 for a net income of $1,734 and for August 1, 1960, through November 30, 1960 sales were $48,758 and net income $2,514. Assuming the sale of all the units being offered, the organizers of the company, H. W. Bobley and E. Bobley, will own 55 per cent of the outstanding common stock of the company and the public will own 45 per cent. Assuming the sale of all the units offered and the exercise of all the common stock purchase warrants, the public stockholders of the company will own 216,000 shares of common stock, or approximately 44.9 per cent; the underwriters will own 25,000 shares or approximately 5.2 per cent and the Messrs. Bobley will own 240,000 shares or approximately 49.9 per cent of the common stock.

Both of these offerings are described in detail in circulars and prospectuses available from the underwriters.

Stock Splits

Procter & Gamble Co. is contemplating an increase in the number of common shares authorized from 25 million to 50 million. Stockholders will be asked to approve this action at a special meeting. The new shares will receive dividends at a rate involving approximately an increase of 7¾ per cent.

Directors of *Revlon, Inc.*, have authorized a two-for-one stock split and increased dividend. Subject to the approval of stockholders, authorized shares will be increased from 5 million to 11 million shares and the new annual rate will correspond to $2.20, compared with the previous $2.00.

WASHINGTON VIEWS

BY JACOB RECK*

87th Congress Gaining Momentum

The 87th Congress, its complexion changed slightly from that of its predecessor, is off and running, now that its "majority rule" squabbles are behind it! The Democrats rule the roost as they have since 1955, but with a thinner majority. One of their own in the White House frees the majority party of a veto threat. Simple majorities will suffice, instead of the two-thirds needed to make controversial legislation hold up under the former Administration. Fears of eroding international confidence in the dollar and the coalition of conservative Republicans and southern Democrats should balk nonessential spending.

Except for early sniping at the outgoing Administration, there will be fewer investigations, now that the same party controls the legislative and executive branches for the first time since 1954. The conservative coalition bolstered by modest GOP gains in the November election, plus the threat of a filibuster, will tend to tone down anti-business trends.

More D&C Controls?

The drug and cosmetic industries will reap some of the whirlwind of last year's Kefauver investigations. During the 87th Congress, there will be a push for additional amendments to provide additional FDA control over the production and shipment of drugs and cosmetics. While the Kennedy Administration is cementing its position, capital seers query and probe to find answers to such questions as, "Who will start the push for more drug and cosmetic controls?" "When will the drive begin?" and "How far will the requests for additional controls go?"

The changeover of administrations provides the drug and cosmetic industries with a welcome breathing spell! There are no reports of industry shedding tears over the departure of former HEW Secretary Flemming. Sensitive to charges of FDA laxity made before the Kefauver Subcommittee, he vied with the Tennessee Senator in proposing drastic, new restrictions on the drug and cosmetic industries. He planned to push vigorously for enactment of his proposals early in this session of Congress, had he continued in office.

Flemming's successor, Abraham A. Ribicoff, the new HEW Secretary, is feeling his way in his new post. He has indicated that he will not emphasize food, drug, and cosmetic matters for the present, but will devote his attention to the Administration's proposals for medical care for the aged and federal aid to education.

For the time being, at least, there will be no upstairs intervention in the activities of the Food and Drug Administration. While Commissioner Larrick recently indicated FDA's legislative program by listing what he called weaknesses in the existing law, FDA cannot initiate legislation or push its program without clearing it with the new Administration. However, much of its program is in the works, as is shown by the recent prediction by Chairman Oren Harris of the House Interstate Commerce Committee on what the drug and cosmetic legislative agenda for the 87th Congress will comprise. Chairman Harris' predictions line up with FDA's indicated legislative proposals which, incidentally, have found their way into a bill (H.R. 1235) dropped into the hopper by Missouri's crusading Congresswoman, Leonora K. Sullivan. To the extent that its budget and facilities will permit enforcement, FDA is expected to recommend amendments to the law proposing:

- A broadened factory inspection to permit FDA to inspect all records, formulas, processes, etc., including those in a consulting laboratory;
- Adequate manufacturing and laboratory controls in drug manufacture;
- A requirement that new drugs be proved efficacious, as well as safe;
- A requirement that antibiotics pass through the certification system;
- A requirement that new therapeutic devices be shown safe and efficacious before they are marketed;
- A requirement that cosmetics be tested for safety and proved safe before they are marketed.

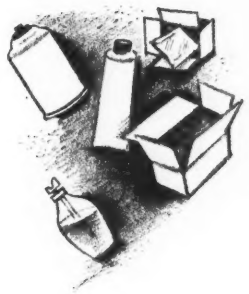
Significantly, in enumerating the legislative proposals to be considered by his House Interstate Commerce Committee, Chairman Harris stated there probably will be a bill providing for the pre-testing of chemicals in cosmetics. Although the Delaney Committee's cosmetic investigations ended almost a decade ago and the perennial Delaney "new" cosmetic pre-testing bill has been introduced in each Congressional session since 1952, the measures have died each session—without even the benefit of a hearing—failing to arouse any enthusiasm or interest on the part of the Congressional leadership. Last Summer, FDA submitted its cosmetic pre-testing bill to the Budget Bureau for clearance, but the legislation was not introduced prior to the adjournment of the 86th Congress. However, Chairman Harris' reference—the first recognition that cosmetic pre-testing controls have received from a committee handling cosmetic legislation—points up the probability of hearings on this measure during the 87th Congress.

Not to be overlooked in running the gamut of legislative proposals is the Kefauver drug control program, which includes provisions covering

(*Continued on page 248*)

*Counsel, The National Beauty and Barber Manufacturers Association.

Increasingly the private label manufacturer is a source of ideas for new products, as well as of the services he has always provided.



PRIVATE LABEL FOR NEW IDEAS

BY RICHARD ANDERSON
SALES MANAGER, STRAND COSMETICS, INC.

Last year a private brand manufacturer created a new product, the liquid eyeliner. It was so enthusiastically received that millions of packages were sold. Sales have now leveled off, yet the liquid eyeliner has become still another staple added to the eye product line. This effective product was developed by a manufacturer who had no extensive research facilities, but who did have an understanding of the impact this product would have on the makeup-conscious public. Other private brand makers are besieged by customers asking for liquid eyeliners, new shades of lipstick, pearlized makeup, and anything "new" that might have merit. What are the factors that make up this great demand for the services of the "private brander?"

Let us go back to 1946, a transition year for toiletries. Wartime shortages of many products, along with expanded purchasing power of the "nouveau riche," public had created greater demand for cosmetics and fragrance. Fringe manufacturers had been selling enormous quantities of inferior products. It was a time when "anything and everything" would sell. Any firm with access to raw materials and packaging could sell whatever it made. Any filler with an alcohol permit could manufacture and sell perfume and cologne. During this period very few new products were born and many standard items could not reach standard quality.

With the end of the war, all of this changed. Retail outlets reduced inventories because their customers lost jobs and purchasing power, and "war baby" manufacturers dropped out of the picture.

Throughout this period, the private brand manufacturer was a bottler or filler, utilized by most toiletries producers only as a source of additional manufacturing capacity. Little imagination was needed by the private brand operator who, for the most part, worked with the customer's formulas and had small need to develop new products.

This situation continued without substantial change for a number of years during which the private label houses sold service, not products. The general sales pitch was: "As private brand manufacturers we will package your products under your label. If you send us your bottles, caps, and boxes, we will put them together more quickly and more cheaply than you can do the job. We are flexible, and can make short runs more cheaply than you can, because our overhead is far less."

With increasing competition in the Fifties, the situation changed and the private brand manufacturer began to offer products. New consumers with new purchasing power had appeared—the wonderful, uninhibited, and imaginative teenagers. They bought the newest lipstick shades; they wore eye makeup and face makeup; they were eager to change their hair styles—even color; they experimented with gadgets and new products; they educated their mothers.

Meanwhile, custom-blended cosmetics became increasingly popular and the franchise line catering to individual tastes became an important factor in the industry. Because the smaller merchandisers in the field often had no manufacturing facilities, they turned to the private brand manufacturer for help. They needed advice about packages as well as about products. They wanted new and different cosmetics; they didn't want to play "follow the leader." They

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GLOBE COURTESY RAND MCNALLY

Foreign markets are tempting more and more United States cosmetics manufacturers.

COSMETICS MOVE ABROAD

BY MILTON MOSKOWITZ

Cosmetics are by no means an American invention, but United States manufacturers today market their products all over the world—with increasing success. The word *cosmetic* is of Greek origin and, according to H. L. Mencken, first appeared in the English language around 1650. However, the words *cosmetician*, *cosmetology*, and *beautician* were all coined in America.

Richard Hudnut is credited with having "first introduced American women to cosmetics," that is, cosmetics as we know them today. The son of a New York drugstore owner, Hudnut became interested in beauty products around 1880. He went to Paris to study the cosmetic and perfume business. After his return, he built a marble-floored store that became America's first beauty salon. He manufactured and sold products under his own name, one of the first being Violet Sec. The Hudnut business was bought in 1916 by the William R. Warner Company, predecessor of Warner-Lambert Pharmaceutical Company. Warner exported the Hudnut line, and today these products are established brands in many world markets. They are, ironically, leading brands today in France, where Hudnut went to learn the business 80 years ago.

This turnabout has become a common occurrence, as U. S. companies seek to penetrate foreign markets. Last year, Revlon, Inc. acquired control of Les Parfums Pierre Balmain of Paris. And in 1959 Revlon obtained U. S., Canadian, and British distribution rights of another French perfumer, Parfums Revillon. French dominance of the perfume business is taken for granted. But how many people are aware that last year the U. S. exported $1,200,000 worth of fragrances, while importing $4,000,000 worth?

The basic reason behind the international expansion of U. S. cosmetic houses is a desire to tap new markets and assure a continued growth in sales and profits. As the standard of living improves overseas, cosmetics become a wanted item. With the tremendous growth in travel and the establishment of common markets among nations, brand names are becoming *international*, with success in one country rubbing off in another country. Success abroad can also be used to good effect in the home market. Northam Warren Corp. ran a major campaign in the U. S. during 1960 to point out that Odo-ro-no is the leading deodorant in "most of the world's fashion capitals."

Compared with Bristol-Myers, the leading seller of deodorants in the U. S., Northam Warren is a small company. But Northam Warren has been pushing its international business for more than 30 years and has built up a healthy volume. Its brand names —Odo-ro-no, Cutex and Peggy Sage—are probably better known abroad than Revlon's. This strong international position undoubtedly attracted Chesebrough-Pond's, which recently acquired Northam Warren. According to some estimates, Northam Warren does more than twice as much business outside the U. S. as in it. As a result, Chesebrough-Pond's, no slouch itself in the international field, may now have more than 50 per cent of its total volume outside the U. S.

The international penetration by U. S. cosmetic houses is not nearly as great as that by their counterparts in the pharmaceutical industry (DCI, January). It is a commonplace now for a drug company to have 25 per cent of its volume abroad. In the cosmetic industry, this ratio is still unusual—although there are some notable exceptions. Drug companies have been mining this area for a long time. It is only in the past ten years that big cosmetic producers such as Revlon and Avon have paid any serious attention to

foreign markets. Also, the marketing problems are quite different. A pharmaceutical producer can capitalize on foreign markets with a drug that is often unique—unavailable from any other source and already tested in U. S. medical practice. A cosmetic product, on the other hand, is much more vulnerable to competition from all sides. There is competition from the local producer, who imitates the U. S. brand, makes a cheap version and sells it at a far lower price. There is competition from British, French, and German manufacturers. The more sophisticated a market, the fiercer the competition. For example, take the Central American countries—unsophisticated markets. You may have a product, say a hand cream, which must sell against five other brands. You may do pretty well and pull down 35 per cent of the market. Fine! However, now take the French market, probably the most rugged cosmetic market in the world. The stakes are high—the French have one of the highest per capita consumption of cosmetics in the world—but the competition is awesome. In France, there are literally 300 different brands of hand cream angling for a share of market. If you take 5 per cent of the French hand cream market, you are doing well, better in fact than the 35 per cent share you are taking in Central America.

If you are entering European markets, you will come up against a bewildering number of brands. Here are just a few: Simoncitron hand cream; Nivea, a German hand cream now marketed all over the world; Kaloderma hand cream; Pantene hair tonic (a Hoffmann-La Roche product to be marketed in the U. S. soon by Chemway); Diploma vitamin hair tonic; Lohse cologne; Uralt lavender water; Penaten baby powder and baby oil; Atrix hand cream; Trilysin hair tonic; and Fauzian's Oriental Beauty Products, which include Fauzia Cream, Fatmila Cream, Gardenia Cream, Peeling Cream, Nile milk with banana, Oriental balm, Oriental green balm,Velvet cream antiwrinkle, Rose cream, Neillifar lotion, Neillifar green lotion, Neillifar camphorated lotion and Day camphorated cream.

Had enough? There are many more.

Despite these risks, many U. S. cosmetic producers are braving the international waters these days. In fact, a few firms, for instance, Elizabeth Arden and Helena Rubinstein, have been important exporters since the early years of this century. The following is a rundown of some of the leading international operations:

Chesebrough-Pond's. This may well be the world's largest international cosmetic operation. Both Chesebrough (maker of Vaseline) and Pond's marketed abroad before 1900. C-P now has distribution in 133 countries and manufactures locally in 48 countries. In 1959, the company did 40 per cent of its $66,-300,000 volume abroad. More significantly, it derived 57 per cent of its $4,000,000 net income from the foreign area. There's a warning here too: Brand names must be protected. In a number of overseas markets the company has lost the right to the Vaseline trademark because it has become a generic term. In some Latin countries C-P markets this product under the Cheseline name.

Warner-Lambert. Another international colossus. Long active overseas, W-L has manufacturing operations all over the world. In 1959, its sales outside the U. S. and Canada rose from $36,634,000 to $39,849,-000, and 32 per cent of this volume was done in cosmetics and toiletries. On these sales the company earned $5,654,000, compared with $4,121,000 in 1958. In addition, the company exported $1,690,000 worth of products from the U. S. W-L derives nearly 40 per cent of its total net income from foreign operations. These operations require a healthy advertising budget. In 1959, W-L spent $41,258,000 on worldwide advertising, of which $9,250,000 was spent abroad.

Max Factor. This West Coast cosmetics house does a handsome business abroad. The company's total sales have skyrocketed from $27,600,000 in 1955 to $53,200,000 in 1959. How much of this has come from the foreign area is a secret that Factor is not revealing. However, industry observers believe that as much as 40 per cent of Factor's volume may now be coming from abroad. In 1960, the company put up new facilities in Australia Germany, England, Italy, and Japan. The company is known to have a particularly strong market position in Britain—at least its share of the British makeup and lipstick markets is a matter of envy for competitors.

Revlon. A latecomer to the international arena, Revlon is now beginning to offer Max Factor a strong challenge in many markets around the world. The company reported that its international sales and

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NEW TRENDS IN TOPICAL THERAPY*

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PHOTO COURTESY DOROTHY GRAY LTD.

I must admit at the outset that in principal I am opposed to the self-treatment of dermatological diseases. The effective and rational treatment of most skin problems requires the counsel of a physician with dermatological experience and skill, a knowledge of the range of therapeutic agents, their action on skin and their specific indications. I am not prejudiced by this viewpoint and will admit freely that some of the modern topical proprietaries are among the most dependable and useful formulas in the dermatologic armamentarium. There are other proprietaries that are less useful. Our common interest, nevertheless, and our common goal is the effective treatment or control of cutaneous disturbances. A natural extension of this common objective is to develop more effective products for use by the physician and the patient.

In the rational therapy of any disease process, we may start by asking ourselves some pertinent questions. What is the nature of the problem—what is the anatomical, biochemical, physiological, microbiological basis of the disease? What is its pathogenesis? And—more relevant to this discussion—what pharmaceutical agents may control the problem when applied topically? *What is the mode of action of the agent? How may it be used and what is the degree of its effectiveness?*

This list of questions might sound like an attempt to over-simplify, particularly since, for many rather common dermatological problems, we do not have adequate answers regarding origin or pathogenesis. Some common ones are seborrheic dermatitis and psoriasis. But even with major gaps in our knowledge, it is possible to control such problems with topical remedies. To be effective, the active component must reach the cutaneous structures affected or the causal agent itself, as in the case of infecting bacteria or fungi. Penetration, or absorption, is therefore an important consideration. In the case of fungus infections of the hair and nails, the obvious reason that topical remedies are relatively ineffective is that the active agent does not get to the major locus of infection in sufficient concentration. In the case of acne, the active agent should, when applied in a lotion or via a scrubbing agent, penetrate to the extent that it will help dislodge the keratin plug in the pilosebaceous orifice and duct, and slow down the pathological reaction at this site.

It is perhaps unfortunate that, in some dermatological and pharmaceutical circles, several pseudo-pharmacological expressions are still used to describe the action of certain topical agents such as keratoplastic, reducing, astringent and stimulating. Keratolysis implies the softening or dissolution of keratin and can truly be applied to only a few chemical agents such as salicylic acid. For the commonly used topical agents such as sulfur, coal tar, resorcin, phenol and mercury, until more specific information regarding their action on the skin is forthcoming, we can only speak of them in terms of their control of

*Presented at the Research and Scientific Development Conference of The Proprietary Association, December 8, 1960, in New York City.

dermatological disturbances, for example, antiseborrheic, antieczematous, or antiinflammatory, agents. This seems crude, but it is more accurate than the pseudo-pharmacological terms which are only misleading.

The large gap in our knowledge of cutaneous pharmacology is not the result of lack of interest. The effective substances about which we have much explaining to do are those agents which have been used effectively for many years on an empirical basis. The attitude has been—we know *that* it works, why bother finding out *how* and *why* it works! It is my personal opinion that research which might cast some light on the mechanism of action of sulfur, mercury, phenol, resorcin, and even salicylic acid might clearly provide new avenues of attack on a a large number of common diseases and even more effective topical remedies might be developed.

So much for terminology and the need for a more fundamental approach. Let us turn to some specific problems.

Acne

Acne is a physiological problem in which we are compelled to treat, not the cause, but the pathologic process in the skin. The increased activity of the sebaceous glands, the plugging of the sebaceous duct and follicle orifice, and the inflammatory reaction around the pilosebaceous unit are the primary events. The cysts and nodules, are extensions of this initial process. When microorganisms gain a foothold, pustules and abscesses occur. Mild acne can be controlled by vigorous cleansing methods and a mild "drying" lotion. I use the word drying with tongue in cheek—it describes the increased scaliness and desquamation, not the decrease in sebaceous output.

For the removal of keratinized epithelium—or the plug, we can employ a cleansing substance (a soap or a detergent) with or without an incorporated keratolytic agent. If we are thinking of using salicylic acid in a cleanser and wish the salicylic acid to remain as the acid (the only form in which it is effective), incorporating it into soap may nullify its activity, since in the presence of alkali from hydrolized soaps the acid is converted to salicylate, which is not keratolytic. A scrubbing agent alone is rarely, if ever, sufficient to control acne. It is an important and useful adjunct to the topical treatment regimen. Sulfur and resorcinol is still the most effective combination of components in topical acne therapy, even though the mode of action is uncertain. Resorcinol may cause a mild inflammatory reaction that results perhaps in peeling. Sulfur may act to oxidize the SH-groups, which may be found in larger amounts in the disturbed epidermal keratinization process, to S-S. Our ignorance about mechanism notwithstanding, the therapeutic efficiency of the combination has been clearly demonstrated.

The choice of vehicle here is of paramount importance. Many proprietaries containing sulfur or resorcin, or both, employ vehicles that are much too occlusive. These include the pancake bases, creams and oil-containing lotions. Occlusive vehicles may promote further plugging and defeat the objective of the medication applied. The most acceptable vehicles are the nonoily lotions. The further criteria for a vehicle are: that it enhance the absorption of the active agents; that it carry a cosmetically acceptable pigment; and that it not be rubbed off easily but may be simply removed with a scrubbing agent. The simplest and oldest of the useful vehicles is an alcoholic "shake" lotion. Any number of modern vehicles are improvements on this ancient but effective base. It would seem contradictory to instruct the adolescent or adult patient with acne vulgaris to avoid oily and greasy cosmetics, but to use a therapeutic agent, which is inappropriate in the same way. This is a major objection to several well-known proprietaries.

Other additives that may be useful in acne vulgaris are antibacterial agents in the cleansing product as well as in the topical medication. This has some application for the patient with secondary infection. I have been incorporating antibiotics in peeling lotions for patients who have a tendency to develop pustules and abscesses. The addition of neomycin may be very useful, (equivalent of 3.5 mg. neomycin base per gm. of lotion). Despite indications for such therapy, there are several cogent reasons why I would not favor the inclusion of antibiotics in proprietary acne preparations. Although bacitracin, neomycin, polymyxin, are regarded as having low incidences of allergic sensitization, this frequency of sensitization might well be increased if the drugs were used indiscriminately over a long period of time. The reports of allergic reactions to neomycin are now well documented. Although the total incidence is still relatively low, this might be swelled considerably by long-term usage. All of the antibiotics cited are also nephrotoxic. Before they can be incorporated into an over-the-counter product intended for prolonged usage, it must be demonstrated that toxic effects will not be produced. Prolonged use may induce microbial resistance to such agents, as well as the overgrowth of microorganisms not sensitive to them.

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TECHNIQUES OF PRODUCT DEVELOPMENT

BY S. V. LIEBERMAN, Ph.D. CONSULTANT

A new product today is too complex to have resulted solely from a single idea or concept; it comes from the combination of thinking, planning, and execution. The underlying or activating concept is the starting point, without which no product will arise, but by its very nature a concept cannot be projected in terms of the work or money to reduce it to commercial practice. The new idea may delight its originator by virtue of its simplicity or complexity, its subtlety or boldness, but to have money value it must be translated into a concrete expression.

There is no standard process for such development of a new product for two industries, or two firms in one industry, or even two projects in one firm. That is not to say that there is no similarity to be found in the development of two different products—there is a superficial resemblance in the over-all processing of an idea to a product, and a surprising recurrence of some nontechnical problems, no matter what the technical nature of the concept and product.

An organization charged with the development of new products will be made up of two general classes of people, technical and marketing. The technical group will include scientists and engineers, laboratory and plant personnel, bench-workers and desk-sitters. We use marketing in a very general sense to include managers and administrators, persons in sales and advertising, assistants and executives. Some technical people operate across the nebulous line, and it is possible to find marketing people who have crossed in the other direction, but, in the main, there are two distinct classes. If each knows and performs its tasks well, there is still no assurance that the product will develop smoothly.

In the product development organizations of today, there is no dearth of communication between the two groups, and each has learned to understand the other. Some problems that recur are due to attempts to make a smooth blend, a happy family, a satisfactory compromise, a unanimous report, a mutually acceptable course—when there is a difference of opinion as to a course of action, compromise may not be the answer. It happens all too often that one is right and one is wrong and any compromise is not right. Such cases call for a clear decision, with the accompanying responsibilities, for one group or the other. Nor is a clear decision for one invariably correct. Sometimes the decision is made by the highest ranking member of the group who may represent one class exclusively (or narrowly), when the decision may have been properly within the province of the other class.

When a concept or new idea for a product has been received, it must be examined critically. This may be done by the whole group after each class has considered it independently. If both approve—meaning that the technical people consider it highly probable that they will attain a product which they will release to marketing, and that the marketing people consider it

highly probable that they will find or create a demand for the product when it is released to them—the group faces its first difficult joint effort. The product must be defined precisely in terms of what the technical people can make and in terms of what the marketing people want to sell and say about the product. The two sets of terms must coincide before any actual work is undertaken. If the technical people cannot guarantee that the product will have a characteristic considered necessary by the marketing people, the latter cannot predict the sales picture. If there really are no alternatives worth examining by either the technical or marketing people, the risk calculators come to the fore. There have been occasions when the "calculated risk" deserved the definition of "a guess by someone who cannot calculate." Nevertheless, reality is a very simple calculation: the probability could be zero, in which case the company loses the cost of the project. If the company is willing (considering other projects in simultaneous process), the project is approved for implementing. If the company is unwilling, the project is abandoned.

Consider how difficult it must be for the proud originator of some concept to accept a verdict of thumbs down. He has a proprietary interest in the outcome of his idea. To keep such a person stimulated, he should be asked to sit in on the group discussion.

There is a gray area, rather than a sharply defined line, separating the province of the technical from that of the marketing. This is most evident in designing products for which more than one specific action is to be included. Whether it is a tablet to carry the miraculous ingredient, a shampoo with the best cleanser, or an antiperspirant without a complaint, it will have characteristics important to the consumer that are not directly controlled by the active component. Marketing will wish to define such characteristics as taste, odor, color, consistency, and even package. The technical men will accept the description of the desired characteristics by the marketing men as goals for their work, but there may be a conflict. There could be problems of compatibility and stability that would give technical prognosticators pause. After the best possible judgment has eliminated many of the possible combinations, there are still more than anyone wants to put into the works. Who gives way? And on what justification? The people with the strongest convictions, the most patience, and the highest rank usually dominate the programming.

We have assumed tacitly that each man always remains within his just province without intruding. The gray area provides some conflict without actual intruding on the other's domain. However, there can be instances when marketing would like to make a stronger claim, or an additional statement enticing to customers, or would just like to see more consumer appeal. All of these are legitimate objectives, and they require formulation changes. What is really at issue are the questions: When is a product acceptable to the group guiding its development? What is involved in cost and time for additional improvements? Will the improvements be justifiable? Will consumers recognize the difference, given a choice? There is no general rule. Where one group might rush to market test, another may drag its feet and make changes, and in other situations these roles could be reversed. The important factor is the recognition of the various courses before any final assessment is made.

Some new products can arise from a description of a need or a demand recognized by marketing. Many technical people have knowledge stored, waiting to be used. There the two must be brought together. The product of research is not directly a new product, but knowledge. It is just as practical and cheaper and quicker, to use existing knowledge in the product development program as it is to uncover new knowledge for the program. If the necessary information is not available, it is the first order of business to outline what is needed, how to get it, and whether its cost is justified. Addition of a highly desirable attribute may have an unusual effect on cost. If the attribute is very desirable, but its pursuit may seriously delay the original program schedule, it should be considered as a separate project.

The selling price of the new product may be determined by factors unrelated to the cost of the major components of the product. Marketing considerations may dictate a maximum price that may be determined by competition, consumer attraction, or future sales volume. After allocations have been made for profit, promotion, distribution, and overhead, the residual amount is available for the cost of producing the new product. In some cases the cost of a proper package may include materials and design that are extra-functional, and the residual amount is reduced considerably. For new products having production costs somewhat larger than the amount that can be allocated, review of all cost factors is imperative. Profit, promotion, distribution, and overhead are usually fixed. If the package contains some extra-functional features, then the package offers a chance for cost reduction. If the extra-functional features were originally included for consumer appeal, they become part of the reason for the selling price, and any

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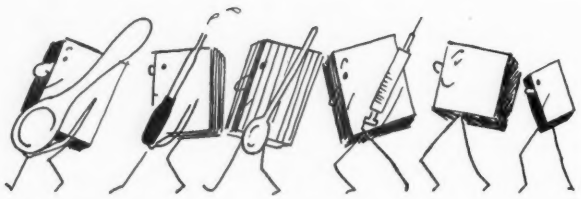
A summary of new drug products issued in 1960, and an indication of the challenge of the new decade.

1960 PHARMACEUTICAL PRODUCTS PARADE

BY PAUL DE HAEN
CONSULTANT TO THE PHARMACEUTICAL INDUSTRY



Knowledge acquired in the past gives direction to discoveries of the future. To take advantage of this knowledge, we must study and review what we have learned, not merely as to the new facts themselves, but also as to their impact on the social environment. New pharmaceutical products and their influence on patients and on society constitute the new knowledge gained every year. To survey what happened in this area in 1960, what group of firms contributed what drugs, and what has been the impact of such products on the practice of medicine and on our society—this is the purpose of this annual review, now presented for the sixth year.

In the last 12 months, the United States pharmaceutical industry has introduced for use by the physician 311 new products, approximately the same number as in 1959. Among these, however, were only 45 new chemical entities, as compared to 63 in 1959. Further analysis shows that the decrease was primarily in the group of derivatives of known chemical structures and new salts of old products. The number of new molecules developed in this country actually increased from 16 to 19. Among these 19 products were four preparations for which a manufacturer had obtained a license either from another manufacturer or from an individual inventor. In this connection we must always keep in mind that the number of new chemical entities marketed in a given year is not a true measure of research activities, because products can be made available for use by the physician only after they have been assigned an effective New Drug Application by the Food and Drug Administration. Concomitantly, all new chemical entities developed in Europe do not necessarily find their way to the American market.

The following chart offers a breakdown of new chemical entities introduced in 1960, the general classification of these products, and their place of origin.

PRODUCTS DEVELOPED IN THE U. S.

	By Manufacturers themselves	By others	Developed in foreign countries	Totals
New and original products	15	4	11	30
Derivatives of known structures	6	1	3	10
New salts of old products	1	3	1	5
Totals	22	8	15	45
Percentage	48.9	17.8	33.3	100

Two of the new, original products developed in this country were synthesized by American research laboratories of firms owned in Europe. These were the important tranquilizer Librium (Roche Laboratories), and the significant hypotensive Ismelin (Ciba Pharmaceuticals).

The preparation of products for analgesia and anesthesia has continued to interest the pharmaceutical chemist. Alvodine (piminodine—Winthrop), a piperidine derivative, is a narcotic effective in low dosage which causes almost no drowsiness or euphoria. It will therefore be welcomed by patients requiring prolonged analgesic therapy. With Analexin (phenyramidol HC1.) Irwin, Neisler succeeded in producing a potent analgesic and muscle relaxant. The search for additional short-acting intravenous barbiturate anesthetics was continued by Eli Lilly & Company, who marketed Brevital (methohexital sodium) in July. This drug, which is one of four isomers isolated, offers the advantage of greater potency on a weight basis, shorter duration of effect, and prompt patient recovery even after large doses for prolonged anesthesia. In Carbocaine (mepivacaine HC1.), Winthrop Laboratories presented a rapid and long-acting local anesthetic.

An indandione derivative, anisindione, was introduced by the Schering Corporation under the name

of Miradon, as an anticoagulant which requires only a single daily administration. The dose is easily adjusted according to the prothrombin time recorded for each patient. Among other cardiovascular agents introduced last year is the potent hypotensive Ismelin Sulfate (guanethidine) of Ciba Pharmaceuticals. The development of this drug is interesting; it was discovered in the course of screening a series of new compounds that promised to be of value in the treatment of trypanosomal infections, such as African sleeping sickness. The discovery of this product is a good example of how careful observations of the pharmacologic action of newly synthesized compounds can unexpectedly lead to the finding of an important, different therapeutic agent. The hypotensive action of guanethidine seems different from that of previously available hypertensive agents, because it acts at the nerve-arteriole junction by opposing the release and/or distribution of the pressor substance norepinephrine. With guanethidine, there is no demonstrable evidence of a central or parasympathetic effect. Reserpine, on the other hand, inhibits norepinephrine through the central nervous system, while ganglionic blockers interrupt transmission of pressor impulses at the level of symphathetic ganglia.

Since the discovery of chlorothiazide (Diuril—Merck Sharp & Dohme), which represented a new approach to the treatment of edema and hypertension, many analogs of this drug have been made. Last year three additional benzothiadiazine derivatives were marketed: Naqua (trichlomethiazide—Schering); Enduron (methyclothiazide — Abbott) and NaClex (benzthiazide—Robins). The claim has sometimes been advanced for the newer agents that they exert less influence on potassium excretion than chlorothiazide, but this claim has been only partially substantiated, and every patient receiving this form of diuretic agent should be watched for potassium deficiency. Several combinations of diuretics with tranquilizers in the form of reserpine and meprobamate have also been offered.

Another nonmercurial oral saluretic and hypotensive of the sulfonamide group, but a phthalimidine derivative, was offered by Geigy Pharmaceuticals under the name of Hygroton (chlorthalidone). In a comparative evaluation of this drug Ralph V. Ford of Baylor University, stated that chlorthalidone "produces less potassium loss than chlorothiazide, has a longer duration of action, and appears to be a significant therapeutic advance." (*Texas J. Med.* **56**:343.) Because of its prolonged action, administration of chlorthalidone may be limited to three times weekly.

Now that we have available an effective hypocholesterolemic agent in the form of triparanol (MER/29—Merrell) the question must again be raised as to whether a reduction in serum cholesterol will bring about a concomitant reduction in coronary artery disease and its sequelae. It may take us five years to obtain a valid answer to this question. It is the present consensus that hypercholesterolemia is not the only factor involved in the genesis of atherosclerosis, but it may be an important one. It seems worthwhile, then, to reduce high cholesterol levels so that we can learn more definitely what influence such action may have on the prevention of atherosclerosis in humans. The administration of triparanol interferes with the final step of the synthesis of cholesterol by the liver and other organs by inhibiting the conversion of 24-dehydrocholesterol, or desmosterol, to cholesterol. The biologic significance of desmosterol accumulation in the serum requires further study and observation.

Two important new antibiotics have been discovered. The synthesis of the first, Staphcillin (sodium dimethyoxyphenyl penicillin—Bristol), was considered an outstanding achievement in an editorial of the *British Medical Journal* of September 3, 1960. Staphcillin is given exclusively by parenteral administration and is not intended for routine use. Its use should be limited to the treatment of infections due to strains of staphylococci resistant to other penicillins, and it fills an important gap in the physician's armamentarium. The synthesis of Staphcillin is a direct outcome of the research that led to the production of 6-amino penicillanic acid, a basic fermentation product from which other penicillins can be made by chemical means.

The other new antibiotic is Humatin (paramomycin—Parke, Davis), for the treatment of amebiasis and bacillary dysentery. Aside from its clinical effectiveness, its interesting feature is its negligible absorption by the intestinal tract. In this respect it resembles bacitracin. Clinical studies made in various countries indicate that paramomycin appears to be an effective amebicide. A new salt of bacitracin,

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PHARMACEUTICAL PRODUCTS INTRODUCED NATIONALLY
1951 — 1960

	Number of firms	Total new products	New single chemicals	Duplicate single products	Compounded products	New dosage forms
1951	86	321	35	74	212	120
1952	89	314	35	77	202	170
1953	107	353	48	79	226	97
1954	101	380	38	87	255	108
1955	124	403	31	90	282	96
1956	126	401	42	79	280	66
1957	127	400	51	88	261	96
1958	126	370	44	73	253	109
1959	106	315	63	49	203	104
1960	109	311	45	64	202	98
Totals		3568	432	760	2376	1064
New Dosage Forms		1064				
		4632				

New single chemicals are new single chemical entities not previously known, and developed by one manufacturer.

Duplicate single products are those, such as dexamethasone or griseofulvin, which are put out by various manufacturers.

Compounded products are those having more than one active ingredient.

New dosage forms are products originally marketed in tablets and now offered in ampuls, suppositories, or the like.

DEVANEY PHOTO

SELENIUM SULFIDE FOR DANDRUFF

BY GAVERN T. WALKER

Dandruff is a very common disorder of the skin. It manifests itself chiefly on the scalp and consists of an incessant production of dry, grayish scales on the scalp, together with accumulated secretions and acquired soil. The scales consist of desquamated epidermal cells.

A very large number of articles and papers discuss this disorder, and it is necessary to state here and now, that there is much disagreement among authorities on this subject as to its origins, its relation to other diseases of the scalp, and its general definition as a clinical condition.

The treatment of dandruff has been discussed by many writers, and there are numerous proprietary preparations now available to the general public. We are concerned here with selenium disulfide in the treatment of dandruff, and we shall not be discussing, therefore, other treatments of the disease.

Selenium disulfide was developed by Nordlander,[1] in the laboratories of the General Electric Company. Nordlander was not a cosmetic chemist; neither was

he a physician with any interest in dandruff. He was engaged in research into materials capable of detecting leakages in mercury vapor turbines, and he found that, by heating one mole of selenium with two moles of sulfur at a temperature of 225° C., the material so formed possessed good stability to light and was chemically reactive.

The possible value of such a material in dermatology was early appreciated by Nordlander, and, after further research, he was able to show that a 1:1 mixture of selenium disulfide and bentonite, after being heated to a temperature higher than the fusion point of the selenium disulfide and finely ground, could then be easily suspended in water, and was active and effective in a number of skin disorders.

Further development of this selenium disulfide type of product led to a still more effective formulation based on the selenium-bentonite mixture, but containing a fairly high concentration of a suitable surface active agent. Such a composition is now well known under the trade name "Selsun," and has proved very useful indeed in the treatment of dandruff. A typical Selsun preparation might contain 2.5 per cent selenium disulfide, 17 per cent surface active agent, 5.2 per cent inert stabilizer, and 75.3 per cent water.

It would appear, from the work of Mattoon[2] at Abbott Laboratories, that the material known as selenium disulfide is not, in fact, SeS_2, since an X-ray analysis of it revealed only crystalline selenium monosulfide, SeS. It was demonstrated further that no new complex resulted on heating the selenium disulfide with bentonite. Although the selenium compound with sulfur would seem to consist of selenium monosulfide, we shall continue to use the term "selenium disulfide," if only to emphasize that the material is prepared by the fusing together of one mole of selenium and two moles of sulfur.

Before discussing the clinical aspects of selenium disulfide, we must mention that studies on its toxicity show that it is comparatively safe to use, having "an ample margin of safety for use under medical supervision."[3] Selsun suspension is, of course, a poison when taken internally, and all Selsun preparations must be plainly labeled as poison.

Since we do not yet know the exact causes of dandruff, we cannot discuss fully the mechanism by which selenium disulfide exerts its effects on the disease. It is well established, however, that the material has both antimicrobial and antifungal activity. Whether such pronounced antimicrobial activity plays a predominant role in the treatment of dandruff is not established. Although some workers believe that the *Pityrosporum ovale* organisms are responsible for dandruff conditions, most authorities today tend to reject this idea. This has been even more notable since the work of Spoor and his colleagues,[4] who demonstrated that the *Pityrosporum ovale* was present in 60 per cent of subjects who were either suffering from seborrheic dermatitis or who were free of the condition. In other words, many normal subjects exhibited the *Pityrosporum ovale* in their scalps.

Although there seems little doubt that Selsun preparations are very beneficial for the treatment of dandruff conditions of the human scalp, there is apparently as yet little real experimental data to support the idea that the action of the selenium disulfide depends on the sulfur, rather than the selenium, although Shair[5] has pointed out that the selenium may well play the role of an intramolecular catalyst by replacing part of the sulfur in the eight atom sulfur molecule(S_8), thus making the sulfur more active physiologically. Whether such activated sulfur could then interfere with the processes that produce the dandruff is not known at present. We need to know a great deal more about the causes of dandruff before postulating mechanisms by which curative agents themselves act on the disease.

Flesch[6] has carried out important work on the effect of Selsun preparations on certain protein material. It would appear that the detergent in the Selsun releases certain nonreactive sulfydryl(-SH) groups, after which the selenium compounds then inactivate some of these -SH groups. It looks as if selenium disulfide played a fundamental part in the bodily functions, although we do not yet know its exact role.

To summarize: We must know more about the causes of dandruff. The biochemist and the physician have much to learn about this condition, but we may look forward with confidence to spectacular advances in the next decade. Moreover, although it is not yet known just how selenium disulfide does its work on the diseased scalp, nevertheless it is certain that this compound is one of the most effective, if not the most effective, means of treating dandruff of the human scalp.

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TABLETTING WITHOUT GRANULATING

BY WALTER KIBBE F. J. STOKES CORPORATION

This dry-blended powder, in a 150 to 200 mesh range, is fed with Stokes' Force-Flo die-feeder at speeds of 2,000 tablets per minute.

A new "Force-Flo" die-feeder for rotary tabletting presses, developed by F. J. Stokes Corporation of Philadelphia, has been described by industry observers who have seen it in action as "the first real innovation in tabletting practice in 56 years." Following more than two years of intensive development, laboratory testing, and production use, the die-feeder has been ordered or is in use by more than a dozen leading pharmaceutical manufacturers.

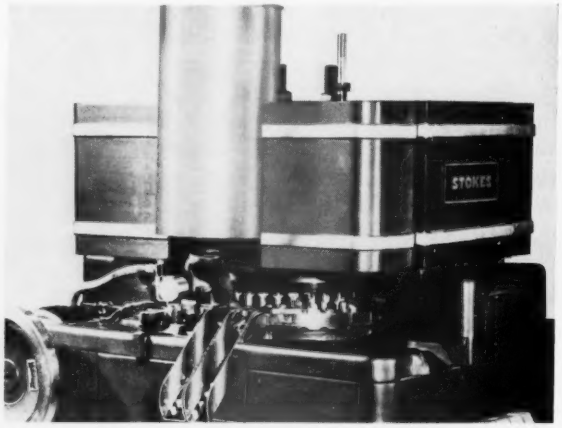
Dry-blended powders can now be fed both smoothly and directly into the press, and efficiently tabletted in a single operation, doing away with the need for wet mixing, drying, granulating, slugging, and other preparatory steps. This also eliminates the need for auxiliary equipment, as well as the operators' art in preparing granulations that flow readily into the press.

In addition, the feeder de-aerates, thereby reducing the bulk of light and fluffy materials. By maintaining a steady and dependable flow of materials moving into the die bores under moderate pressure, it minimizes air-entrapment and consequent laminating and "capping" in the finished tablets. Its action also increases the density of the tablets, leading to consistently higher and more nearly uniform quality.

With the Stokes "Force-Flo" die-feeder, new formulations that otherwise would not feed satisfactorily can be tabletted. Consequently, heat sensitive mixtures requiring a dry binder can be fed more easily into the press or the slugger. The device also efficiently feeds wet-process granular or semi-granular materials that would otherwise feed sluggishly.

Tablet hardness is controlled by varying the pressure adjustment of the press. With most granulated materials, 10 per cent more can be fed into the die with the Force-Flo than before; a harder tablet of the same weight consequently results from lower depth-of-fill. Fine powders with more points of contact will lead to firmer bonding than is the case with coarser granulations. Powders instead of granules also result in more nearly uniform density, color, and texture in the tablets. Finally, not only does elimination of equipment for granulation and slugging result in substantial savings in capital investment, but doing away with these steps also reduces the cost of direct labor.

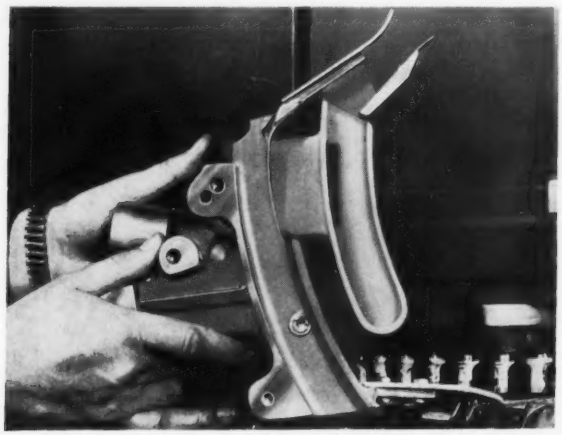
In tests, 150 to 200 mesh material, similar in texture to common flour, was successfully fed at speeds of 2,000 tablets per minute, using $\frac{3}{8}$-inch punches and dies. Total weight variations were 3 to 4 per cent, or + $1\frac{1}{2}$ to 2 per cent. A free-flowing granulation at this speed would be expected to show a total variation in tablet weight of between 5 and 6 per cent. Some semi-granular materials have been fed at speeds



Die-feeder allows semi-granular materials to be fed at speeds up to 5,500 tablets per minute, with weight variations kept within close limits.

of 5,500 tablets a minute, with total weight variations of less than 3 per cent.

The new Stokes die-feeder is a simple, self-contained attachment whose principal element is a specially designed, feed frame that is interchangeable with the standard fed frame and can be installed on the press, or removed from it, with the same ease as a standard feed frame. The special feed frame consists of a closed floating shoe with a built-in power unit. The shoe is mounted on the feed frame by means of special rubber pads, making it stable around its vertical axis but free to move in the horizontal plane.



Closeup of underside of floating shoe of die-feeder, which is over die bores, showing opening for proper re-circulation of overfilled material.

The hermetically sealed power unit uses compressed air to generate a continuous orbital movement of the shoe in the horizontal plane. The shoe is moved an exact amount, horizontally and in the proper direction, to coincide with the rotation of the rotary head of the press for the most efficient feeding action.

The frequency of the movement of the shoe can be adjusted over a wide range (to suit the particular material being tabletted), simply by increasing or decreasing the air pressure. This high-frequency movement of the entire shoe provides a surface to which no material will adhere. Neither the intensity of the movement nor the length of time that material remains in the unit is enough to separate the ingredients, but it is sufficient to de-aerate the material to the equivalent of a tapped density .The connection between the top of the shoe and the hopper is vented to allow air to escape.

The partially closed aperture at the bottom of the shoe is positioned directly over the open die bores for almost the full length of a standard feed frame. The rotation of the rotary head of the press pressurizes the material in front of the partially closed aperture of the shoe, forcing it into the die bores. Over-filled material is ejected from the die bores with a standard weight-adjuster cam at the trailing end of the feed frame, just as in conventional frames. This spill-out takes place in front of the partially closed aperture. The excess material is recirculated around the die table and returned to the open end of the shoe.

Thus, the new die-feeder performs two functions: It applies a moderate amount of pressure to the material as it goes into the die bores, and it accelerates the flow of material through the feed-shoe. Hence the aptness of its name, Force-Flo.

The other element of the die-feeder is a compact and attractive control box, which is mounted at the rear of the press, and houses dial gages for indicating the air pressure and simple controls for easy and accurate adjustment. It also includes a safety device to stop the press automatically, should the air supply falter or be accidentally cut off.

Unlike mechanically agitated devices, the Force-Flo die-feeder has no moving external parts to come in contact with the material being tabletted. This means that there is no chance of contamination of the finished tablets by metal chips or flakes, as might be the case with devices having spinning agitators, and the like. Moreover, there is no need for elaborate magnetic inspection devices. Also, there are no separate mechanical drive units, wires, switches, plugs, or such, to fail in service and generally to clutter up the operating area. Finally, there are no bearings to bind or become worn and cause misalignment, and,

Closeup of the new Force-Flo die-feeder. Here, it is installed on a Stokes model 551 51-station, high-speed rotary tabletting press.

consequently, there is no need for lubrication, another possible source of contamination of the finished tablets. Virtually no maintenance is required. •

COSMETIC REACTIONS AND

BY HOWARD T. BEHRMAN, M.D.

ASSOCIATE PROFESSOR AND DIRECTOR OF
DERMATOLOGIC RESEARCH, NEW YORK MEDICAL COLLEGE

This paper by Dr. Behrman is the first to appear of the six presented at the Sixth Symposium on Cosmetics co-sponsored by the Committee on Cosmetics of the American Medical Association and the Section on Pharmacy of the American Association for the Advancement of Science, held in New York City, December 29, 1960. We have arranged with Dr. Joseph B. Jerome, secretary of the Committee on Cosmetics, to publish all of the Symposium papers.

Dr. Behrman here discusses the incidence of reactions, and the types of preparations that cause them. He states, at the very outset, that the number of persons who develop reactions from cosmetics is fairly small, and that the preparations generally available today are quite innocuous.

In the over-all picture of an active dermatologic practice, a certain percentage of skin reactions due to cosmetics is encountered. Although various estimates of the frequency of cosmetic dermatitis have been put forth, an exact listing of the actual number of cases is not only difficult but well nigh impossible. Why should this be? The primary reason is that the average person who uses a cosmetic and develops a skin reaction merely discards the cosmetic and either uses another brand or none at all. A small percentage of these people will consult a doctor, usually a general practitioner who does not report such cases statistically. An even smaller percentage will consult a dermatologist or a skin clinic. Depending upon the severity of the reaction or the state of their pocketbooks, a few will seek legal retribution, and some will write to the manufacturer, a federal agency or a medical society. It is only from the last few sources that we can compile our statistics, and so our records are unfortunately inadequate. However, we do have some knowledge as to the more common offenders, and my purpose is to review the subject of cosmetic reactions and their significance. The number of persons who develop reactions from cosmetics is fairly small and the preparations generally available today are quite innocuous.

Incidence of Cosmetic Dermatitis

For reasons already mentioned, it is difficult to give an exact estimate of the incidence of dermatitis due to the various cosmetics. This could only be ascertained in a dermatologist's testing paradise, where a community of several thousand individuals would be constantly bombarded with all the new cosmetic applications over specific periods of time under the most rigidly controlled situations. In the event that some dermatologist replaces Krushchev as the next Russian premier, such a community might be established, but I'm afraid that the practical limitations of our working democracies confine us to the statistics available. Let us glance at some of these.

In a 1937 study,[1] approximately a thousand patients exhibiting some form of dermatologic disease were patch tested. Reactions to cosmetics were obtained in 3.8 per cent of those tested. This does not necessarily mean that their skin disease was due to these cosmetics, but that they were allergic to some of the ingredients in these cosmetics. The cosmetics producing these reactions in their order of frequency were: face creams, rouge, lipsticks, face powders, and eye cosmetics.

In a more recent study[2] of 25,000 patients with eczematous skin reactions, only 2 per cent of these

people were sensitive to a cosmetic product as verified by patch testing. In this group the order of frequency was: creams, lipsticks, face powders, hair dyes, and nail lacquer. A major cosmetic company summarized its experiences[3] in cosmetic reactions as compared with the unit sales of its products. In this study, the highest incidence of reactivity was shown by depilatories, with an incidence of 3.9 reactions per 100,000 units of the preparation sold. The company's next five leading dermatitis producers were, in the order of frequency, special cleansers, permanent wave lotions, hormone creams and lotions, and medicated creams and lotions. All this is interesting but somewhat confusing.

Let us take a slightly different look at the situation of statistics by narrowing the field down to the causes of dermatitis of the eyelids.[4] Dermatitis of the eyelids is often due to contact with cosmetics and, since the

skin of the eyelids is very sensitive, it often gives a rapid evaluation of allergic reactions to external agents. In one study of eyelid dermatitis, Hazen[5] stated that approximately 30 per cent of his cases were due to cosmetics, with nail polish as the primary offender, followed by face powder and facial creams. However, 10 per cent of his cases were due to fruit peel and he included other such exotic offenders as insecticide spray, fly bite, and sensitivity to dogs' hair.

Another series of cases of dermatitis of the eyelids was reported in Denmark.[6] In this group, less than 25 per cent of the cases were due to beauty preparations. None of these patients were allergic to nail polish, but nail polish is not used routinely by Danish women. As a matter of fact, Danish women use fewer cosmetics than do their United States counterparts. However, a large number of these women had reactions to potted plants. In this modern era, it seems as though American women spend more time at the beauty parlor or with their psychiatrist than they do with potted plants, and so we see more examples of dermatitis of the eyelids due to cosmetic and emotional factors—this is a much more expensive hobby than indoor gardening.

THE CLINICAL DERMATOLOGIST

Another report stems from Swinney[7] of Texas, who found that cosmetics were by far the most common cause of eczema of the eyelids and, in his series, the most frequent offenders were cream base shampoos. With all that oil spouting in the air over Texas, these women probably have to wash their hair more often. Finally, let us review an excellent study[8] from France by Sidi and Mawas. In their large and well-controlled study, the largest group of cases of dermatitis of the eyelids were due to contact with therapeutic solutions and ointments used around the eyes. This occurred in 50 per cent of their patients. However, cosmetics were a close runner-up and produced 35 per cent of the reactions, of which the majority were due to nail polish, eyelash makeup, brilliantines, and hair dyes. Of course, here we are dealing with French women, who are extremely beauty conscious and would be expected to have a higher incidence of cosmetic reactions.

Where do all these studies lead us? They lead us to the conclusion that the incidence and types of skin reactions to the various cosmetics differ according to the country, the examiner, the type of usage, the availability of statistics, and many other variables, making an exact tabulation impossible. According to Rostenberg,[10] of the cosmetics in common use, the ones most likely to produce allergic reactions are: (1) oxidative hair dyes, (2) lipsticks, and (3) nail polish. He has also stated that antiperspirants are most likely to produce mild irritative reactions. In my own experience, the most common offenders are depilatories, hair dyes, nail polishes, lipsticks, and antiperspirants.

Causal Mechanism

Dermatitis due to cosmetics is primarily of an allergic, contact type.[9] This means that the cosmetic does not cause an inflammatory reaction of the skin when it is initially applied, but only after it has been used for some time. This time lag, usually referred to as an incubation period, is often a week or longer. In other words, a cosmetic that is harmless to most people, produces an allergic response in the skin of a susceptible user only after it has been repetitively applied.

To explain why this should happen would necessitate an explanation of the fundamental mechanisms of allergy beyond the scope of this report. However, a simple explanation advanced by Rostenberg[10] lucidly stated that the two major factors in the genesis of any sensitization are: (1) the intrinsic allergenicity of the compound, and (2) the genetic constitution of the host. These two factors are inversely related, so that if one is small the other must be large in order for a sensitization to develop, and this explains why most people do not develop a dermatitis from the average cosmetic. Another way of stating this would be that a powerful sensitizing agent in a cosmetic could overcome a comparatively mild allergic tendency in the user or, conversely, an extremely allergic individual could react violently to a weakly sensitizing cosmetic. These facts also substantiate our clinical observations that more people become sensitized to hair dyes than to face creams, and that people who are allergic to some cosmetic often react to other cosmetics. Inasmuch as the hereditary background

of the cosmetic user cannot be altered, the manufacturer can only be of help by selecting materials of a low allergenic potential. As Rostenberg observed, chemistry will no doubt provide means to predict the strong sensitizers, that is, those that are most likely to cause a sensitization in a great number of people; but it is dubious that in the future it will be possible to foretell the occasional individual who, for reasons that are quite obscure, becomes sensitized to some substance to which most of his fellowmen are indifferent.

Although allergic contact dermatitis is by far the most common type of cutaneous reaction resulting from the use of cosmetics, it is not the only type of reaction encountered, and the others will be mentioned for the sake of completeness. A second causal mechanism is that due to contact with a primary irritant in a cosmetic. By definition, a primary irritant is a substance that will produce a dermatitis on first exposure, in any one exposed to it for a sufficient length of time. For example, sulfuric acid is a primary irritant. Fortunately, very few cosmetics contain primary irritants and then only in very weak concentrations. However, a primary irritant may also be a sensitizing agent and, in a person allergic to it,

even very small amounts of the chemical may produce a dermatitis. For example, potassium dichromate in a concentration of 100 per cent is a primary irritant and will produce an acute dermatitis in any normal skin, whereas in a concentration of 0.25 per cent it will not affect a normal epidermis. However, the 0.25 per cent concentration may produce a dermatitis in individuals who are sensitized to it.

Still a third type of dermatitis from cosmetics is due to contact with a chemical that makes the skin sensitive to sources of radiant energy such as sunlight. The usual example of this type is the so-called Berloque dermatitis due to the oil of bergamot contained in some perfumes. This dermatitis is manifested by a brownish pigmentation of the skin after exposure to sunlight following an application of some substance containing the perfume oil. Brownish tear drops and streaks along the course of the perfumed cosmetic usually make clear the diagnosis for the examiner.

Another type of pigmentary cosmetic reaction follows long usage of a substance such as mercury, with a resultant local deposit of this heavy metal and a bluish black pigmentary change.

The Most Common Cosmetic Offenders

1. *Depilatories.* Most depilatories in use at the present time contain calcium thioglycolate in a cream or lotion base with a *p*H of approximately 12. A few contain sulfides of barium or calcium. These creams are capable of producing a mild degree of primary irritation rather than an eczematous sensitization. These irritative reactions are more likely to occur if the depilatory remains on the skin for too long a time, or if they are applied to more sensitive areas of the skin such as the face. Careful adherence to the manufacturer's directions will usually avoid trouble.

2. *Hair Preparations.* Most hair dyes contain oxidation-type coal tar chemicals such as paraphenylenediamine and paratoluylendiamine and, when first introduced, the incidence of reactions was quite high. At one time the Federal Food and Drug Administration stated that out of every 1,000 persons who used this dye, 15 would become sensitive to the first application and 25 would sooner or later acquire sensitivity with continued use. Formerly, these oxidative dyes were not only classified as potent sensitizers, but were capable of producing various types of toxic reactions as well. Within the last five years, however, the incidence of reaction has become quite low, even though these dyes are used more extensively. This may be due to improvement in the quality of raw materials, including the peroxide, better quality control, improved techniques for the oxidation of paraphenylenediamine, and more caution on the part of the hair dresser and the consumer; the probability is that greater caution on the part of the hair dresser (use of preliminary patch tests as required by the FDA) has been responsible for the lower incidence of reactions to hair preparations. The other types of hair dyes, including henna and other members of the vegetable group, the metallic hair dyes, and the sulfonated azo dyes, are usually less satisfactory dyeing agents, but have a smaller incidence of cosmetic reactivity. Cosmetic sensitization may also occur from the cold wave lotions, the active ingredients of which are thioglycolates, and from hair lacquers, which on occasion have produced dermatitis of the face and eyelids. This occurred in a group of women using a spray in which a synthetic resin was substituted for the shellac. Allergies may also occur from the polyvinylpyrrolidone extender, the shellac, and the propellant. Hair shampoos and the various hair tonics and lotions may also produce cosmetic reactions. (*Continued on page 251*)

33 BECOME 13

Every pharmaceutical manufacturer is eager for the means to reduce filling machine changeovers, to decrease down time considerably, to minimize adjustment changes for different kinds of seals, to reduce inspection costs and record keeping, and to gain closer inventory control and minimized storage requirements.

Pfizer Laboratories and J. B. Roerig and Company, sales divisions of Chas. Pfizer & Co., Inc., have found a way to do all this, by standardizing their bottle line. It was no small task to package all existing dosage forms in fewer bottles, but only 13 bottles now handle the packaging load that formerly took 33—those shown in the background above.

Until this standardization, the Pharmaceutical Products Manufacturing Department at Brooklyn was forced to stock 33 bottles in almost as many shapes, diameters, and heights for the packaging of tablets, capsules, liquids, and powders. Varying in capacity from a tiny four-cc. vial to a 200-cc. size, these containers required scores of seals and cartons in dozens of different sizes. Moreover, they all had to be readily available for production lines, which meant considerable storage space. Clearly, a complete streamlining of bottles, closures, liners, labels, and cartons was required to bring about any real savings.

The complicated job fell to Hugh Horner, head of Packaging Design, Jerry Lott, also of that department, and Frank Michel of Process Control. It was up to them to eliminate, retain, or design the flint and amber-colored bottles. In this they were aided by extensive studies in packaging and distribution, as well as by specialized engineering and quality control equipment, including a newly developed concentricity gauge.

The 13 new bottles bear a strong family resemblance in their wide mouths and contour shoulders. Moreover, although the capacity range is still about the same, there are only five body diameters requiring only four seal sizes—a sharp contrast to the former 29 diameters and 11 seals.

The new bottles are taking the place of the older ones as present inventories are depleted, and Pfizer expects immediate economies in several ways.

In the first place, the carefully calculated size and capacity ratios of the new line call for fewer filling machine changeovers. Obviously, set-up time will be reduced, since the number of complex adjustments to be made on the high-speed filling and sealing machinery will be considerably reduced.

A standard bottle neck for the entire line allows the application of either roll-on or pilfer-proof seals with equal facility, and with little time out for most adjustment changes.

Inspection costs will be reduced, as will record keeping, and, since bottles will be brought in from the supplier only as needed, inventory control will be closer and storage requirements lessened. Further, quantity purchases of the millions of bottles used each year can be made more conveniently, with a consequent price advantage.

Finally, an improved identification system greatly facilitates ordering. A code designation on the bottom of each of the 13 bottles identifies the type of dosage form and bottle size: For example, L-60 indicates 60 cc. of liquid; Y-90, 90 cc. of dry fill.

Pfizer may not be especially interested in one other result, namely a precedent for other companies, but this seems very likely to us. *G.M.S.*

PHOTOGRAPHY BY DICK BOYER

BERNARDIN closures keep good company!

Brand Preference is the expression of customer satisfaction earned by a product over its competitors. We like to feel that our relations with "French's Mustard" likewise confirms the expression of the several satisfactions a closure must provide "on the line," during shipping, at the retailers and in the consumer's hand. *May our Closure Craftsmen work with you?*

SINCE 1881 · BERNARDIN BOTTLE CAP COMPANY, INC., EVANSVILLE, INDIANA

Packaging and Selling

What a challenge there is in the packaging industry today! What profound and deep changes are on the threshold, and what tough competitive struggles face this dynamic industry!

The packaging industry, in all its branches—packaging materials, the fabrication of the multitude of the packages, and packaging and material handling equipment—have had a dozen or more magnificent years. These have been creative years with countless improvements and new inventions in packaging, as well as years in which packaging has been an essential part of our social and economic life and has revolutionized American marketing and the American system of distribution.

Now, however, anyone reading the news and looking at the releases is conscious that a change is due. This does not mean any slowup in creative inventions and improvements. As a matter of fact, it seems obvious that the new things that will come out in packaging will appear in accelerated quantity and in startling improvements and innovations.

It does not mean any less dependence on the part of the American enonomy on packaging but, undoubtedly, an increase in the part packaging will play in our economy.

It does mean, for one thing, that the basic material producers for the packaging industry—that is, steel or more properly, tin plate, and all its variations; aluminum with its various methods of application and treatment; paper in an infinite variety of forms; plastics, a great industry in itself; and glass—are all entering into a period of excess factory capacity in which the colossal battle of these materials against each other will intensify.

The fact is that, in many applications, practically all of these products are in direct or indirect competition. It is perfectly possible for steel, aluminum, plastic, glass and sometimes even paper, to be in direct competition for a package or a packaging part.

Although steel is doing a great deal of research and coming up with interesting variations, and aluminum in its various forms and surface treatment is presenting an increasingly interesting material, and glass is also producing some interesting improvements, the fact is that paper and plastics are the locus of the revolutionary changes in packaging.

Plastics are such a diversified field of completely different materials that almost anything or any problem seems capable of finding a solution here. The chief buyer of our leading cosmetic company recently remarked that he expected within five years that all of his company's packaging problems would be solved within the plastic industry. The new perfume purse flacon of Carven Parfums, made in an injection mold from liquid nylon and complete with gold, is to us an astounding new product. This container is as tough and rigid as glass or metal, it is practically unbreakable, its metal plating is as beautiful as anything that can be done on metal, and yet it is of feather weight, a quality which a recent survey showed was most demanded by women for purse flacons.

In the paper industry almost anything can happen. Right now, it is doing astounding things by combining paper with other materials, for paper bags and paper containers, even more astounding things in forms of unwoven fabrics for throw-away material and surface treating by coating paper with other materials.

While all of this ferment is an exciting challenge to the packaging industry, as well as a promise of some tough competitive headaches to come, it also opens up fascinating vistas for the industries that use packaging.

Both the pharmaceutical and the cosmetic industries, which have so many records of great sales successes based partly or primarily on a package, must look with new interest and new alertness to what will be happening constantly from now on among the packaging people.

Economists seem to agree that in 1961 the cost of living will show a slight increase. The trouble with opinions of this sort is that they are almost always formed on some such statistic as, for instance, in this case, the Consumer Price Index.

Our only objection to the Consumer Price Index is that, like the figures on steel operating ratios, it is not always a true reflection of what is taking place.

For instance, a few years ago the Index was boosted a fraction of a point when New York City increased subway fares from 10 cents to 15 cents. At that time, automobile workers in Detroit got a pay raise because this fraction gave them a new cost-of-living boost. Then again, it is on the record that Hurricane Donna gave quite a boost to certain food prices, which moved the Index up several fractional points, although a large majority of Americans may not have been eating any of the foods effected by this hurricane.

As a final criticism, we do not think the Bureau of Labor Statistics has quite caught up with the dis-

With DAVIS ACETATE sheeting...you can stop losing sleep over your packaging!

The makers of Geritol and Sominex lost no sleep over packaging! They asked for the utmost in brilliant, eye-compelling appearance for these two hard-selling products... and they got it!

Western Printing Company filled the bill with the dramatic bubble packages pictured above...using extruded acetate sheeting by Joseph Davis Plastics Co. to achieve sparkling clarity and crispness.

Davis extruded acetate sheets, rolls and film come in all gauges — transparent, translucent, or opaque — and are ideal for vacuum forming.

We have been advising industry on plastic packaging for over 40 years, and we would welcome the opportunity to help you. Let us send you a brochure on our facilities and the wide range of plastics we produce, together with their properties and applications.

PRODUCTS BY J.B. WILLIAMS CO., PACKAGING BY WESTERN PRINTING CO., EXTRUDED ACETATE BY JOSEPH DAVIS PLASTICS CO.

JODA

Joseph Davis

PLASTICS COMPANY

430 Schuyler Avenue, Kearny, N.J.

Phone: WYman 1-0980 New York: BArclay 7-6421

count houses and price cutting in general, which is really lowering the cost of living for a whale of a lot of people in the United States.

It was bound to happen, because this is the age of the computer. Anticipating by a little bit the computing method of determining whether a new product will succeed, Curtis C. Rogers, president, Consumer Panel Division Market Research Corp. of America, has come up with a method of employing advanced mathematics to predict new product performance.

The actual procedure is far from being as formidable as the title would indicate.

In this mathematical method, three sets of facts are required: (1) The rate at which customers are trying the product; (2) the tendency on the part of customers to make repeat purchases, and the time interval between purchases; and (3) the amount purchased at a time.

When a new product achieves the first degree of market introduction and perhaps some success, it has reached a substantial number of tryers. These people cannot be called confirmed customers because they merely show a willingness to sample the product.

When, at the beginning, a new product has attracted a fairly large number of samplers, marketers often get a false feeling of optimism, but the truth is, if the product is to flourish, adequate numbers of tryers must be converted into repeat buyers.

Lack of repeat buying is probably the major cause of failure of new products, that is, excepting those few that continue to depend on one-time purchasing.

Even a second purchase does not indicate that a customer will come back again and again. Novelty products frequently show a high level of initial repeat but very little thereafter. Thus, repeat buying must include the subsequent purchasing beyond the first or second or third repeat.

According to this study, there are some indications that the rate of repeat buying may be inherent in the product when it is launched.

Even though there is some possibility that the repeat rate may change, this does not alter the fact that the original repeat rate of the product is a definite key to future success. However, a product can have a large number of tryers and an adequate repeat rate and still not be a success. The amount of time that elapses between purchases of the product may be so great that only a small volume will be obtained in any one period of time. Thus, if the frequency of purchasing is not sufficient to produce adequate volume, the manufacturer's course of action is somewhat limited.

The third factor, that is, the amount the customer buys at one time, depends, of course, on the size of the package, whether it is a multiple package and frequencies of that sort.

Of course, in this mathematical method of computing, certain factors must be assumed. For instance, that the distribution will not greatly shift; that the promotional expenditures will not be substantially different; that the price will not show a marked charge; that the product will not be reformulated or changed materially; that the package will not be redesigned in a major way; and that competitive activity will not substantially change.

From there on, it is a matter of advanced mathematics, and out of the formula at the end will come a prediction on the success of your new product.

Rare indeed is the product that starts off such a chain reaction of competition as has Metrecal.

Now, apparently, that competition is diversifying and spreading into new fields—we hear that Hance Bros. & White Co. long established pharmaceutical company is test marketing Soup-R-Cal, a 900-calorie hot soup for weight control. This product, we hear, is being sold through the Walgreen's drug chain in Chicago and is being launched with a full-page co-op news ad.

Of course, we do not think that this is by any means the end in the dietary weight control field. If our Philadelphia friends make any sort of success with Soup-R-Cal, you can be sure that Mr. Heinz and Mr. Campbell and a dozen others will pile in in a big way, just as the dairy companies have been jumping into Mead Johnson's back yard.

The really big clash will probably come when the liquor industry spots this field. We do not see any reason why there should not be a line of weight reducers spearheaded by a product that might be called Martini-Cal.

In our opinion, some of the most delicious flavors in the world are ready at hand, in this particular industry.

The Glass Container Manufacturers Institute expects glass containers to reach 170.1 million gross in 1961, an increase of 7 per cent above estimated 1960 shipments.

A gain of 12 per cent is expected from medicinal and health glass containers, which are expected to reach 24.3 million gross. Demand for toiletries and cosmetics is expected to reach a total of 14.8 million gross, a gain of 7 per cent.

This is a very healthy estimate for expansion for this industry next year.

The susceptibility of the consumer to a sense of smell, as well as that of color and other factors, in making a sale will soon be tested by a leading supermarket, the Grand Union.

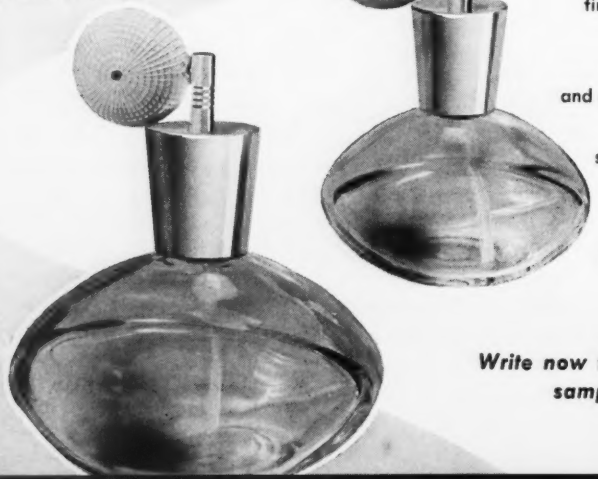
In this grocery retail store, coffee, strawberry, and apple pie scents will be produced by an electric aroma dispenser. The cost is said to average between $20 and $30 a month per store with a wide range of aromatic food odors.

INTRODUCING . . .

the new FANTASY Pagoda

BOTTLES CAPS

. . . attractive and imaginative glass containers to give your product glamorous eye-catching appeal! Available immediately from our unique "in stock selection" in ½, 1, 2, 3 and 6 oz. sizes with the standard neck or with Richford's fabulous spillproof feature. Topped off with the handsome Pagoda Cap in gleaming Goldcote or black, your product will be enhanced by this exceptional package!



. . . Futura Atomizer Caps in brilliant Goldcote® or Silvacote® finishes to compliment the Fantasy Bottle. Designed to give your product "plus value," these unusual and outstanding containers and caps are available in 2 and 6 oz. sizes with gold or purple atomizers.

Your Product Deserves

RICHFORD CORPORATION

Write now for samples and prices.

Executive Offices and Plant
3618 Oceanside Rd., Oceanside, N. Y.
Showrooms
Empire State Bldg., 350 5th Ave., N. Y., N. Y.
Sales offices in all major cities throughout the wo

The recent Christmas season did produce some highly original co-op ads, particularly among the perfume companies. One that came to our attention and received particular notice in the office was the Tabu advertisement run by Bonwit Teller in Philadelphia.

This was a half-page with a headline, Give Her Tabu and Really Sleigh Her!

Dana's hypnotic fragrance
is guaranteed to break the ice;
but if she's already thawed . . . woo, woo!
A single drop behind
each ear, and she'll become Tabu
to everyone except you.
But if she wears it all over
. . . woo, woo again!
Ooey, what a powerful expression
of love this is!

It is interesting to hear why other executives fail, but if you are an executive yourself, it is much more interesting to keep from failing yourself.

The Stevens Institute of Technology, which has made quite a feature of personal appraisal, recently came up with eight reasons for executive failure, conclusions based on a study of 300 executive failures. Executives fail because they: (1) Don't delegate authority; (2) lack breadth of knowledge; (3) can't analyze and evaluate; (4) can't judge people; (5) can't cooperate; (6) can't make decisions; (7) don't have drive; (8) lack responsibility.

The Ladies' Home Journal will publish this year a series of 12 articles on "How America Spends Its Money."

The first article in the January issue is a detailed study of the cost of living of an American family with a yearly income of $5,803.20. That figure is the mid-point in the income for America's 44 million families.

This family has a weekly expenditure for medical care, medical insurance, and life insurance of $5.42, and an expenditure for personal care of $1.22.

In another table, which gives the breakdown of monthly expenditures, income taxes come to $53.77, food, $120.60, clothing, $19.60, medical care including health insurance, $17.12, and personal care including hair cuts and cosmetics, $5.30.

Industrial designer Walter Landor believes in taking a good look at a package design. He recommends the following viewpoints.

(1) *How does your package look from 12 feet?* Does it stop the eye first, ahead of all competitive products on the shelf; does it convey the feeling of the product it contains even before you are near enough to read brand and commodity; does your package in mass display command the consumer's attention by setting up an intriguing visual pattern leading the eye from package to package?

(2) *At arm's length?* Does your package have maximum impulse purchase appeal; does it look the best buy in relation to apparent quality and size; do your brand *and* product names achieve instant recognition without cancelling each other out in their bid for the consumer's eye?

(3) *In your hand?* Does it inspire confidence; does it look as if a sound, reliable firm is behind it; does it look like the best quality in its price class; does it have a plus feature, the merchandising extra in design or copy which makes the housewife feel you really have her interest at heart?

(4) *In use at home?* Is your package nice to have around, does its design "wear well" compared with competition; is it easy to handle, store, open, use; is its design personality strong enough to make people remember it, and reach for it next time they are in the store?

Mr. Landor thinks that seven out of ten will come out of this searching session sensing that all is not well.

The dram container, which was once important in the cosmetic counters of leading department stores and enabled American women to buy their choice of perfume for a price between $1.50 and $3.00 a dram, has practically disappeared from the American scene. American women now almost universally buy the fragrance of their choice as cologne or in a purse flacon.

During 1960, the Rollarama stepped into a gap left by the disappearance of the dram flacon with a series of very attractively designed metal containers, which could easily be filled by the customer from any fragrance which they happened to have at the time by means of a small funnel, a part of the Rollarama package.

This metal flacon has a roll-on method of application for the fragrance, which gives easy application.

It does seem as if a great many people in the ethical pharmaceutical branch of our industry are re-appraising their advertising policies and the way in which they spend their money. It seems to us that every new issue of an advertising journal has a news note about a change in advertising policy.

Just recently we were interested to read that one of the leading pharmaceutical companies has decided to discontinue its own medical publication, and a few weeks later another leading pharmaceutical company announced that it would, for the first time, issue its own journal.

Another trend that may be in the making is the way certain ethical companies are developing a specialty that lends itself to consumer advertising and consumer merchandising. Apparently, in certain products of the trade, notably vitamins, the competitive pressure is so intense that in spite of the attitude of these companies toward the AMA, they still

THE LADY PREFERS

. . . glass containers that compliment her good taste every time she uses the product. Here is a modern classic in a stock design. Its very simplicity gives it an elegant, luxurious air . . . an air that spurs impulse sales.

Available in a wide range of popular sizes . . . clear, frosted, or sprayed in ceramic color . . . undecorated or with applied ceramic label.

Specify Design #100 . . . prove to yourself that glass stimulates sales.

CARR-LOWREY GLASS CO.

designers and manufacturers of fine glass containers

FACTORY & MAIN OFFICE: BALTIMORE 3, MD.
NEW YORK OFFICE: 415 MADISON AVE.
CHICAGO OFFICE: 1572 MERCHANDISE MART

feel compelled to go to the public for this division.

Last year Squibb launched a substantial advertising campaign with a typical consumer pitch for its Vigran vitamins. Now we hear that Upjohn has appointed a leading advertising agency with an appropriation substantially exceeding a million dollars in consumer media for its Unicap vitamins.

It is, of course, common experience that mail order, house-to-house, and nationally advertised vitamins have been growing fantastically in sales, at the expense of a great deal of the ethical business in this field.

The fact to be determined, however, is whether these enormous sales increases are based on a substantially lower price, or whether it depends on that particular form of marketing.

According to the torrent of press releases announcing new mergers, acquisitions and expansion projects, we are coming into a period of tremendous activity in plastics. Everybody seems to be getting into the newer extrusion field and, as far as we can tell, there will be more companies making plastic- extruded bottles next year than any other type of container.

No matter what happens to business, prepare for a year of extraordinary activity in new packaging developments.

We have felt for a long time that we are entering an era where hardly anybody will have the color hair that their ancestors set aside for them. American chemistry is doing such a wonderful job in hair coloring that there is no reason why the American woman, who is now so meticulous in matching such things as purses, gloves and shoes, ought not to match the color of her hair with every new dress or purse or shoe or glove she acquires.

It seems, however, that the English people have taken quite a big jump on us in this respect. A recent newspaper account from Wisbech, England states, "A boy without pink hair is a boy without a girl friend."

This new teen-age rage got started when one boy had his hair sprayed with a pink solution. "At first the girls laughed but now they won't go out with any boy who hasn't got pink hair."

This spray apparently need only be applied every two weeks. "The only trouble," said one of these bold pioneers, "is that on chaps with dark hair the solution tends to turn their hair scarlet."

It appears that a number of industries are discovering the sales and promotional value of traveling girls. In a recent issue of an advertising publication an article apeared with a heading, "How to Use Traveling Girls for Promotion." This article had quite an enthusiastic description of this apparently new method of selling.

It is undoubtedly true that the cosmetic industry has the longest, the most varied, and the most thorough experience in using traveling women, not only for selling and demonstration and educational work, but for local publicity. The way in which these women have been used has taken highly specialized forms.

The most common use of traveling women in the cosmetic industry has been for planned demonstration periods and public appearances in stores that did not justify the use of a permanent, paid demonstrator.

Traveling women have also been very widely used in the cosmetic trade as field sales managers and for educational purposes in conducting schools and courses for salesgirls in retail stores.

Normally these women are highly trained, highly competent sales people who have come up through the selling ranks, either from a retail store or in a manufacturer's sales department. However, there have been countless variations.

Several years ago Lancome experimented with carefully selected French girls with unusual success. These girls spoke English with a very attractive French accent, were extremely intelligent and vivacious and nice looking, and made quite a substantial hit in every store and city they visited.

It was something of a problem to maintain these several girls because unusual precautions were taken to protect them in the way they traveled, in hotel accommodations and so forth. It was estimated that total cost for each of these girls ran from $15,000 to $20,000 each.

Right now, Chanel is using a limited number of highly selected publicity and public relations women with unusual success in stimulating local publicity.

In spite of the effectiveness of this method of selling, even in some cases the extraordinary effectiveness, there is little likelihood that there will be too big a development in this direction. The reason for that is that the cost of these traveling women is almost always superimposed upon an already expensive sales department and a bursting advertising appropriation. Except for a very specific and important program, the cost is just a little bit too much to add to current sales expenses.

Growth and profits still depend to a large extent on the development of new products. Chemway, whose earnings this year have been less than expected, has great expectations for next year, according to Charles T. Silloway, the company's president.

The new high-priced imported cosmetic line, Biotherm, is expected to make a substantial contribution to volume in 1961.

Chemway is also test-marketing Pantene, a men's hair lotion, and after shave lotion. These products are on license from a Swiss drug company and are large sellers in Europe. Also on license is a new protective hand cream for women to be used before washing dishes and doing housework. This is a West German license.

Task-Designed seamless Spra-Tainers are an exclusive Crown development. With neither side seams nor shoulder seams, the Crown Spra-Tainer permits greater propellant pressure, protects volatile products better than any other aerosol container.

Only Crown—pioneer in the aerosol field and the leading producer of aerosol cans—offers you both seamless and fabricated cans. And only Crown gives you the benefit of so much experience, so much research. Crown production facilities are Task-Designed to meet your needs, promptly, efficiently and accurately. Please write for more information.

CROWN *for cans · crowns · closures · machinery*
CROWN CORK & SEAL CO., INC., 9300 Ashton Rd., Philadelphia 36, Pa.

NEWS IN PACKAGING...

1. North Brite, a new paperboard material made from a homogeneous blend of virgin pulpwoods, has been introduced by the Packaging Corporation of America. It is a solid sheet providing superior strength with thinness, light weight, and a fine printing surface.

2. Winners in the Ninth Annual Aerosol Package Awards Competition selected from over 270 entries: Gillette Right Guard Deodorant; Chesebrough-Pond's Seaforth Minute Shave; Breck Hair Set Mist; Faberge's Esprit de Parfum; Blackman's One For a Man Spray Cologne; Wallace and Fiernan's Desenex Aerosol Foot Powder (not shown).

3. The Mennen Company has redesigned its tube shaving cream products by incorporating the new logo into a simpler design of blue-green and green on a white background. A glossy finished board has been used for the carton. Design—Francis Blod Design Associates, Inc.

4. Bradley-Sun Division of American Can Company has designed a high-density polyethylene tube for dental impression material. The low-heat conductivity of polyethylene allows the tube to be handled with bare hands after immersion in boiling water, for easy dispension.

5. Product and display card can be combined with a seemingly invisible film that is applied so that the product is self-standing, hung from pegs, or stacked on shelves. The stretch-pak, by Nevins Company, combines stretchable polyvinyl chloride film and paperboard.

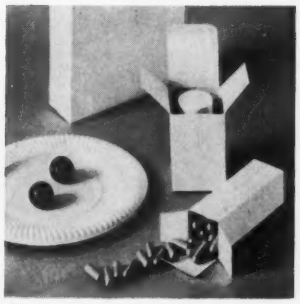
6. Edith Rehnborg's cologne mist is in a 3-oz. clean looking container by Peerless Tube. The loading was done by Western Filling of Los Angeles. The trigger top actuator cap is by V.C.A. and Metal Fabrications.

7. Simonetta's Incanto spray mist cologne is in an aerosol 1-oz. container with a black and white silk-screen design suggesting ancient Roman ruins, designed and produced by Risdon Manufacturing Co., filler Powr-Pak.

8. Corrugated expendable pallet, called Econo-Pal, designed by the Packaging Corporation of America, can be assembled from one piece of corrugated board to provide a low-cost and easily transportable base, capable of carrying strapped loads as heavy as 10,000 pounds.

9. Campana Corporation has discarded its carton and introduced redesigned bottles in three sizes with a harmonious gold foil label. Miniature carton replicas are being affixed to the new bottles during an introductory period. Bottles by Owens-Illinois, labels by Wheeler Van Label Co., neck tags by Normandie Press.

10. Kirby-Cogeshall-Steinau Company's counter display unit for Denney and Denney holds 42 items in palette style trays, using slightly more than one square foot of counter space, and showing color range.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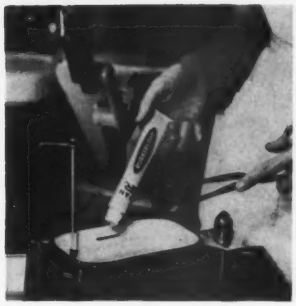
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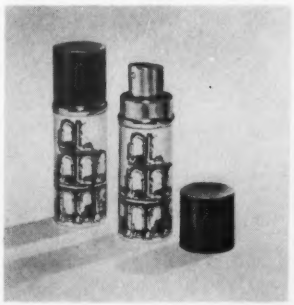
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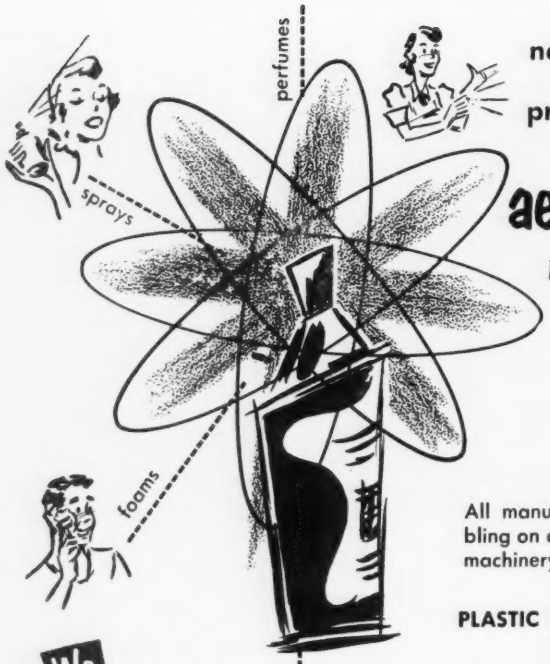


new IDEAS and new products...our STRENGTH

aerosol packaging

AND NITROGEN FILLING

SPRAYS . . . FOAMS . . .
METERED PURSE-SIZE AEROSOLS

- PRODUCT FORMULATION
- PACKAGE CREATION
- QUALITY CONTROL

All manufacturing, packaging, and assembling on continuous-flow production lines . . . machinery and connections of stainless steel.

PLASTIC TUBES & CONTAINERS FILLED NITROGEN FILLING

We . . .
FORMULATE
MANUFACTURE
PACKAGE

Old Empire

HUmboldt 4-2121
N.Y.C. WOrth 4-7870
865 Mt. Prospect Avenue, Newark 4, New Jersey

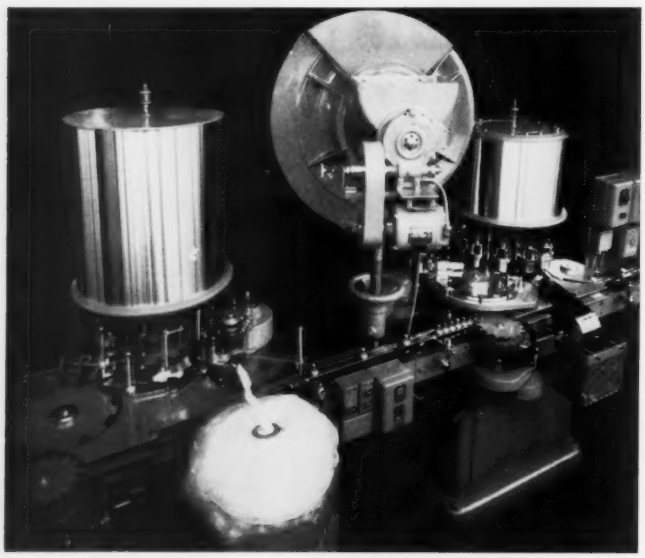
Old Empire

PERFUMES & COLOGNES
LIQUID & CREAM SHAMPOO
TOOTHPASTE
HAIR PREPARATIONS & SPRAYS
DEODORANTS
SHAVING CREAMS
SKIN PREPARATIONS
CREAM RINSE
HAND PREPARATIONS
BATH PREPARATIONS
OINTMENTS
PHARMACEUTICALS

Wad your containers with the

CONSOLIDATED KOTTONER

Your most efficient equipment for Automatic Bottle Wadding



Consolidated KOTTONERS will speed your production and reduce your costs in wadding pill, capsule and tablet containers with either standard or "inverted U" type of inserts. Capacities range from 40 to 310 wadding operations a minute with complete synchronization not only with CaPeM capping equipment but with all other related units. Cotton weight may range from 3 to 22 grams.

While the principal application of Consolidated KOTTONERS is with smaller packaging units — from 25 to 100 by count or from ½ to 6 ounces by size — they can frequently be adapted to other requirements. In any case, the satisfactory experience of hundreds of users proves that you will find the Consolidated KOTTONER the finest of all automatic wadding equipment. It will serve you economically and efficiently for years to come.

For complete information and quotations, write outlining your needs and send us filled and wadded samples of all size containers to be handled.

Model KL-10-TB Consolidated KOTTONER (left) in use with Model D-10-F CaPeM Capping Unit.

CONSOLIDATED PACKAGING MACHINERY CORP.

1400 West Avenue • Buffalo 13, N. Y.

A Subsidiary of International Paper Company

NEWS and VIEWS

BY TED KLIEN PUBLIC RELATIONS DIRECTOR*

207 Per 100,000

If you need a doctor, live in Boston. Among the greater metropolitan areas with populations of a million or over, the Boston area has the highest ratio of physicians to population, according to a report issued recently by the Public Health Service.

In the four counties that comprise the Boston-Lowell-Lawrence metropolitan area, where the ratio is highest, there were 207 active non-Federal physicians per 100,000 people in mid-1959. The San Francisco-Oakland area (made up of six counties) ranked second, with a physician-population ratio of 199. The consolidated New York-northeastern New Jersey area (which links eight New York counties with eight counties in New Jersey) was third, with 189 physicians for every 100,000 persons.

Drugs in Sweden

In the December 1960 issue of *The Journal of the American Pharmaceutical Association*, Hans Hellberg, head of the National Pharmaceutical Laboratory of Sweden, writes an excellent summary of how his country directs the flow of prescription drugs. Since the Scandinavian countries have had long experience with socialized medicine, the article presents some interesting facts on how such a program actually operates. Since Mr. Hellberg recently has spent three months in this country observing how we distribute drugs, his observations are all the more relevant.

He explains that "all hospitals are run by the state or by local communities. Our general and compulsory health insurance provides for the cost of hospitalization in a common ward or the cost of a private practicing physician up to certain maximum fees. If we want to consult a more expensive doctor or if we want care in a private room in the hospital, we have to pay the additional cost ourselves. Drugs prescribed by a physician are also in part paid for by health insurance."

Those drugs needed by patients suffering from chronic diseases like diabetes, heart disease, and asthma are completely paid for by the state. However, he writes that for "other prescribed drugs our insurance pays part of the cost. Because health insurance has reduced the cost of medicines to the individual, there may have been an unnecessary increase of drug consumption in Sweden. I think most people agree, however, that the benefits outweigh the disadvantages."

Hazards of the Trade

Advertising Age, that chronicler of the quick, now comments on the dead. In a recent issue, the trade publication of advertising reported that the average age of death in 1960 for admen was 60. This average has been the same for about three years. (Some reference points: The physician's average age when the maker calls is about 69, as is the dentist's.) The life expectancy for most Americans is about 70.

Now I ask you, why does the man who sells something live for a shorter time than the one who buys it? Is there nine years of difference in spending your life trying to find ways to interest buyers in someone's merchandise? Or is the reduced life expectancy due to the fact that the very nature of the business lends to making the pace so fast that only the strong can survive, and then for not very long?

It seems to me that we in the advertising business made a choice long ago—the very selection of this career has, as a hazard of the trade, tension, conflict, and a continual race with the clock; deadlines, client meetings, creative conferences; and, then, almost as quick a pace when we relax. We rush out to the golf course, race through evenings at the theater so we can catch the 11:15 p.m. to Stanford, and rush to bed to sleep a fast six-and-a-half before the 7:45 a.m. to Grand Central.

We who toil in the vineyards of advertising should know that we are giving up almost a decade of living when we decide to stick to our career. It's worth it for most of us, but I wonder if our clients know the price we pay.

DCAT Symposium

A highlight of the year for the venerable Drug, Chemical and Allied Trades Association is their annual Waldorf Dinner. On March second of this year something new will be added. It's a full-day symposium on "New Challenges in Health, Welfare and Business."

The dinner is expected to draw over 2500 members and their guests. Many will also attend the symposium, but nonmembers are also invited to hear the various discussions of the symposium without having to attend the dinner.

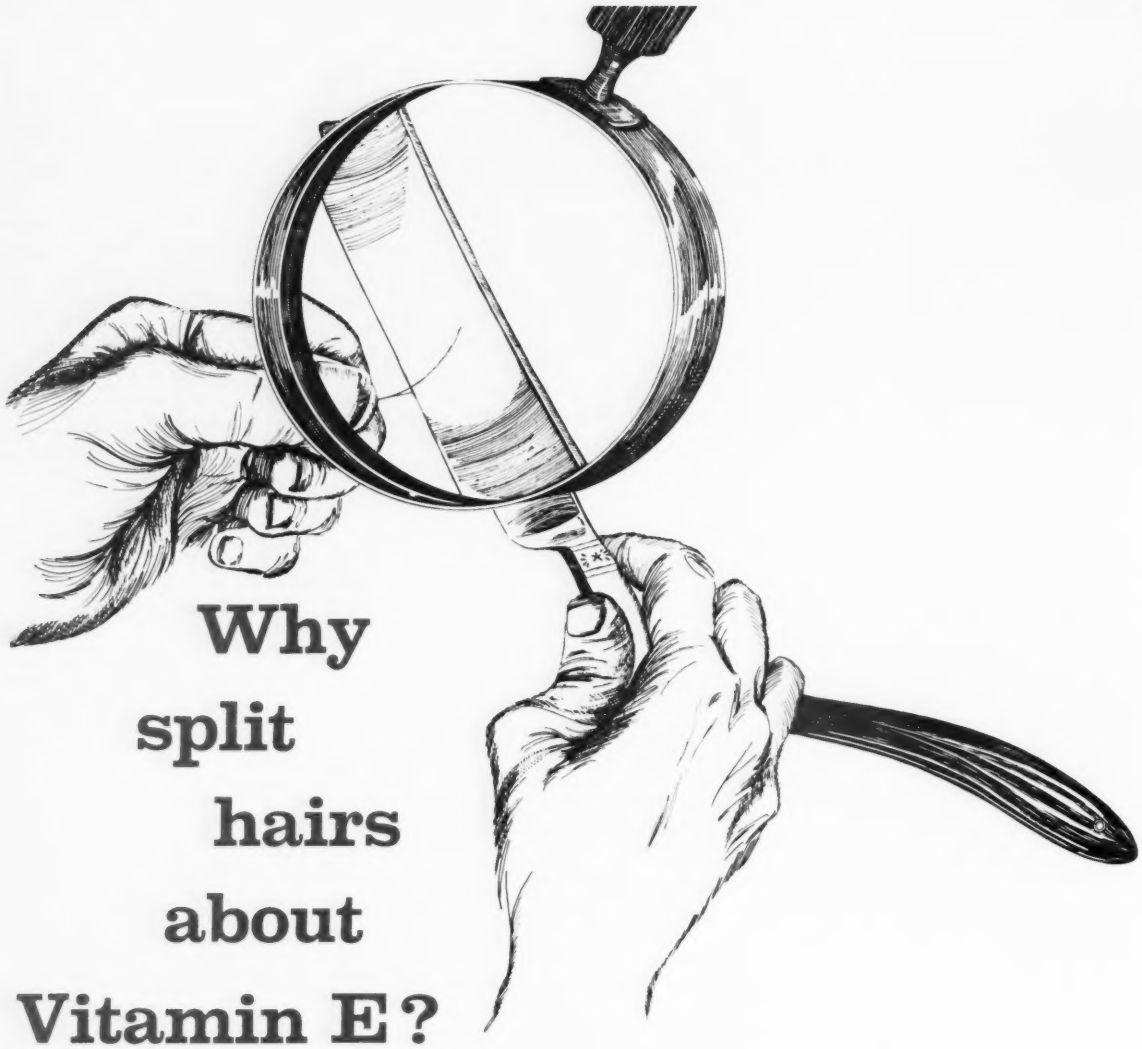
Lead-off speaker for the symposium will be John E. Fogarty, Rhode Island Congressman, who is proud to be called "the champion of better health for the nation." He is the man responsible in large part for increasing the National Institutes of Health appropriations from $3,500,000 in 1946 to better than $590,000,000 in 1961.

Roland J. Dahl of Squibb is symposium chairman, and Dr. John N. McDonnell of Schieffelin is co-chairman for the full-day program. They have organized three continuous conferences, to follow a morning address by Representative Fogarty.

Starting at two o'clock and running for about two hours, these conferences have been planned to probe deeply into subjects close to the industry. The titles of the conferences, which will include a panel discussion, are: "Industrial, Academic and Governmental Research — Competitors or Collaborator?"; "What Is Industry's Responsibility to the Public Welfare?"; and "How to Meet Competition—At Home and Abroad."

All members of the DCAT are invited, as well as any who feel that the symposium will add to their knowledge of the industry and its problems. The date, Thursday, March 2, 1961; the time, morning session 10:00 through 11:30 a.m. In the afternoon, the three conferences will be held simultaneously beginning at 2:00 p.m. A fee of $5.00 per person will be charged for sessions. Additional information can be obtained from Helen Booth, DCAT Secretary, 1 Liberty St., N. Y. C. 5.

*Paul Klemtner & Company, Inc.



Why split hairs about Vitamin E?

Vitamin E is Vitamin E. It has to be.

- A unit is a unit.*
- You buy a unit.
- You pay for a unit.
- You label it a unit.

A unit of E is a unit of E
No matter what the kilo cost may be;
The unit cost is based on parity.
Type makes no difference, as you can see.

*THE RECOGNIZED INTERNATIONAL UNIT OF VITAMIN E IS 1 MILLIGRAM OF DL-ALPHA-TOCOPHERYL ACETATE, ADOPTED IN 1941 USING ROCHE VITAMIN E FOR THE STANDARD.

Get your Vitamin E *right* from Roche.

FINE CHEMICALS DIVISION **HOFFMANN-LA ROCHE INC.** Nutley 10, New Jersey

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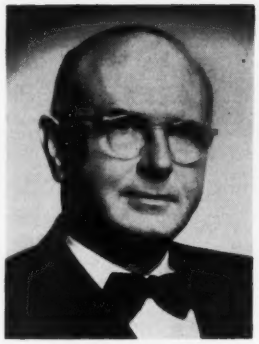


ARTHUR C. EMELIN

WAYNE HICKLIN

RICHARD E. BAITER

LEON GIVAUDAN

NEWS...

Appointments and Promotions

Arthur C. Emelin, president of Wallerstein Company division of Baxter Laboratories, Inc., has been elected a vice-president of the parent company. Since joining the division in 1958, Mr. Emelin has directed a research program for new products, a stepped-up marketing program, and policies designed to foster good employee and community relations. **Albert M. Juergens, Jr.,** formerly with American Cyanamid Company has joined Wallerstein as Mr. Emelin's assistant. **Frank K. Beck has been appointed** sales promotion manager of Baxter He was formerly with Wade Advertising, Inc. of Chicago as marketing coordinator.

Six executive appointments have been made by Avon Products, Inc.: **Wayne Hicklin,** vice-president, sales, is now senior vice-president; **Norman Chadwick** succeeds him as vice-president in charge of sales; **Clifford Winton,** national district sales manager is now vice-president in charge of merchandising and promotion; **George McGowan,** vice-president; and **Hays Clark,** who had been head of manufacturing at Avon's Morton Grove Laboratories, is now vice-president in charge of international operations. **Wilbur R. Shook,** formerly treasurer at Worthing Corporation, has joined Avon as treasurer, succeeding **Louis W. Jaeger,** who has retired. Mr. Jaeger continues as a consultant to Avon.

Richard E. Baiter has been elected marketing vice-president of the Pepsodent Division of Lever Brothers Company, succeeding T. E. Hicks, who continues as vice-president. Previously Mr. Baiter had been merchandising manager of the Division.

Leon Givaudan has joined the executive management of L. Givaudan & Cie., S.A., Vernier-Geneva, Switzerland after having spent eight years in charge of the development of Cia. Brasileira Givaudan. He continues active in its management.

Northam Warren, Jr., has been elected president and chief executive officer of the Northam Warren Corporation, succeeding his father who founded the firm in 1911. He has also been elected a vice-president of Chesebrough-Pond's Inc., parent organization.

Bristol Laboratories has appointed **Victor T. Johnson,** formerly vice-president and director of marketing, as administrative assistant to the president, Philip I. Bowman. **Thomas E. Watson** succeeds Mr. Johnson as vice-president and director of marketing. He has been manager of market planning since January 1959.

Eli Lilly and Company has announced four new appointments. Filling newly created positions as executive directors are **Ralph C. Gery** in pharmaceutical production, and **Robert E. Heine** in production services. **Joseph E. Marmon** has been elected group vice-president of manufacturing and administration, and **William R. Spurlock,** group vice-president of marketing and subsidiary operations.

Frederick J. Zimmermann has been elected vice-president in charge of plants and engineering for Sterling Drug, Inc. Mr. Zimmermann will continue to head two Sterling divisions, Salvo and Zimpro. **Charles C. Wood** has been appointed vice-president in charge of sales for Sterling's new subsidiary, Breon Laboratories Inc. The Glenbrook Laboratories Division has announced three new sales executive appointments: **Charles K. Brown,** national accounts manager; **A. J. Galloway,** drug trade sales manager; **W. Earl Goodrich,** vice-president in charge of sales. **Frank W. Millard** has been promoted to assistant product manager of Glenbrook.

John L. Pausch has been appointed vice-president in charge of finance in a newly created position at Warren-Teed Products Company. Mr. Pausch was previously with Dresser Industries, Inc.

E. C. Slaght, Jr., has been appointed vice-president and technical director of Newport Industries Division, Heyden Newport Chemical Corporation. The former manager of market development will organize and co-ordinate the company's expansion and new product programs.

William Weston has been appointed executive vice-president of Ultra Chemical Works, Inc., subsidiary of Witco Chemical Company, Inc. Mr. Weston, formerly vice-president in charge of operations, has been with Ultra for 22 years.

Paul P. Woolard, formerly vice-president, marketing, has been named executive vice-president and a director of Prince Matchabelli Inc., subsidiary of Chesebrough-Pond's, Inc. The subsidiary has also named **Frank H. Orr,** executive assistant to the marketing vice-president, as assistant to the president.

John P. Cusano, formerly general manager of Purdue Frederick International, has been appointed vice-president of the company. Before joining Purdue in 1959, he had been northeast regional manager of Pfizer Laboratories.

DAVID BENJAMIN

RAYMOND L. MAYHEW

JAMES A. TORRENS

ROBERT M. WATKINS

David Benjamin has been appointed vice-president of Aerosol Techniques, Inc., in charge of planning and engineering. Mr. Benjamin joined A.T.I. in 1957 as director of purchasing and has recently been assistant to the president.

Raymond L. Mayhew has been appointed to fill the new position of manager of technical service and development at Antara Chemicals, General Aniline & Film Corporation. With GAF since 1944, Dr. Mayhew was recently program manager in charge of chemical specialties. GAF has announced three appointments in the research and commercial development department of the chemical group. **Francis J. Prescott,** formerly supervisor, sales development, is now manager, market development. **Albert Bloom,** with the company since 1946, remains manager of business research for the Dyestuff and Chemical Division. Helen M. Schleiter has been appointed assistant to Dr. Knowles, manager, commercial development. L. Byron Cherry has resigned as general manager of the company's Ozalid Division.

James A. Torrens, who has been with the Toni Company, division of Gillette Company, since 1946, has been named general sales manager. For the past two years Mr. Torrens has been national field sales manager. **Robert F. Bryant** and **William F. Frost** now hold two newly created posts in the sales division, Mr. Bryant as assistant general sales manager in charge of sales force field operations, and Mr. Frost as assistant general sales manager for field development.

Bristol-Myers Products Division has appointed **Robert M. Watkins** product manager of the new products group in its marketing department. **J. Richard Edmondson** now holds the newly created position of assistant secretary for Bristol-Myers, and **Floyd R. Baughman** and **Augustus W. Kelley, III,** have both been made assistant comptrollers.

Robert A. Nielsen has joined Estee Lauder Cosmetics as general sales manager. Mr. Nielsen had been sales manager of Parfums Givenchy and Parfums Millot.

Roger M. Kirk, Jr., sales manager, has been named manager of the Lehn & Fink Division of Lehn & Fink Products Corporation.

William P. Broas, formerly sales director, is now vice-president for the Warner-Lambert Products Division of Warner-Lambert Pharmaceutical Company, and **Gib Dannehower** a product director of Bromo Seltzer.

The research and development department, Canco Division, American Can Company, now has four divisions: the Research Division, headed by **Dr. Orval R. Alexander;** the Technical Service Division with **Donald W. Riester** as general manager, **Richard R. Hartwell** as assistant, and **Donald J. Wessel** as manager, Central Laboratory; the New Products Division, retaining **Alden J. Schneider** as general manager; and the Machinery Development Division, with **Albert O. Morkish** continuing as general manager.

The Warwick Wax Division of Western Petrochemical Corporation has established a west coast sales distrct in Pomona, Calif., with **Lyle Christensen** as district sales manager.

Martin C. Sampson, M.D., has joined Schering Corporation as director of medical relations. He has been associated with affiliates of Schering since 1958. **Edward J. Holder,** formerly with Continental Can Company, has joined Schering as sales training manager.

William H. Rorer, Inc., has appointed **Charles H. Steeper,** with the company since 1958, as Seattle district sales manager.

Harry W. Fritts, formerly packaging section manager, has been appointed development manager, containers and packaging, a new position in the Aluminum Company of America's new development division.

Walter Kneip, formerly sales representative for Tygart Valley Glass Company, has joined Brockway Glass Company as Virginia district sales manager.

Fred H. Stewart has become director of the tablet and capsule manufacturing department for Strong Cobb Arner Inc., where he has been since 1957. **Malcolm F. Hurd** has been appointed a buyer for the firm.

G. I. Roberts, D.V.M., has joined Burroughs Wellcome & Company's marketing and advertising division with responsibility for all professional service work relating to veterinary medicine.

John J. Horan, director of public relations, has been transferred to executive director of administration for the Merck Sharp & Dohme Research Laboratories Division. **David F. Quinlan,** who joined Merck in 1958 as manager of communications, succeeds him as manager of public relations. **Jack Blodinger** has been named technical service assistant in the medicinal products department, Merck Chemical Division. Before joining Merck, Mr. Blodinger was with American Cyanamid Co. for 13 years, the last six in the Lederle Laboratories Division.

G. W. BOYD

L. E. GAINES

WILLIAM N. ARDUSER

VICTOR M. LEVEY

Several changes in the company's organization have been made by Emery Industries, Inc. **John M. Archiable,** works manager for 13 years, is now director of foreign operations and corporate director of the manufacturing staff. **R. F. Brown** is now general manager of the Organic Chemicals Division, and **G. W. Boyd,** general manager of the Fatty Acid Division. Mr. Brown and Mr. Boyd have both been sales managers of their divisions.

L. E. Gaines, formerly with Plax Corporation, has joined Continental Can Company as sales manager for the Plastic Bottle and Tube Division.

William N. Arduser, manager of the scheduling and planning department of the Toledo Mould Company, division of Thatcher Glass Manufacturing Company Inc., has been promoted to production manager.

The Felton Chemical Company, Inc., has appointed **Victor M. Levey** research director. Mr. Levey, formerly technical director of Tragacanth Importing Corporation, has published several papers of microderivatization of organic compounds, and on natural gums.

Robert E. Tyriver, formerly manager of national syndicate stores and military sales, has been appointed sales manager of the Charles Antell Division of B. T. Babbitt Inc.

Dr. Erwin Klingsberg has been appointed a research associate at the American Cyanamid Company research center. Dr. Klingsberg, with Cyanamid since 1956, is now studying the properties of a family of sulfur compounds discovered by him.

Dr. John G. Salsbury has replaced his father, Dr. J. E. Salsbury, as president of Dr. Salsbury's Laboratories. His father continues as chairman of the board. **J. E. Price,** purchasing; **J. A. Haase,** finance; **Dr. O. H. Peterson,** research; **R. H. Cooper,** production; and **H. G. Bos,** marketing have been named vice-presidents in charge of their departments.

Maurice A. Deane, vice-president and advertising manager, has been appointed general sales manager of Endo Laboratories.

Francis M. Beudert, formerly with Miller Brewing Company, has been appointed director of sales, and **Eugene J. Milano,** formerly with Bristol-Myers, director of Metrecal marketing planning for the Edward Dalton Company, a division of Mead Johnson & Company. **O. B. Walker** will be director of Pablum-BIB marketing planning and **Robert E. McMillan** will be director of new product marketing for Dalton.

John B. Ellis, professional service representative, has been appointed sales manager of the south Atlantic region for Organon Inc. **Dick Kuschinsky,** with Organon since 1952, has been appointed director of professional services.

Dr. Walter G. Kunze has been appointed process development associate and **R. B. Evans,** scientist, for the research and development group at National Starch and Chemical Corporation. Dr. Kunze is a recognized expert in destrin manufacturing and, together with Mr. Evans, has developed new methods for the derivatization of starch and new techniques for making starch films.

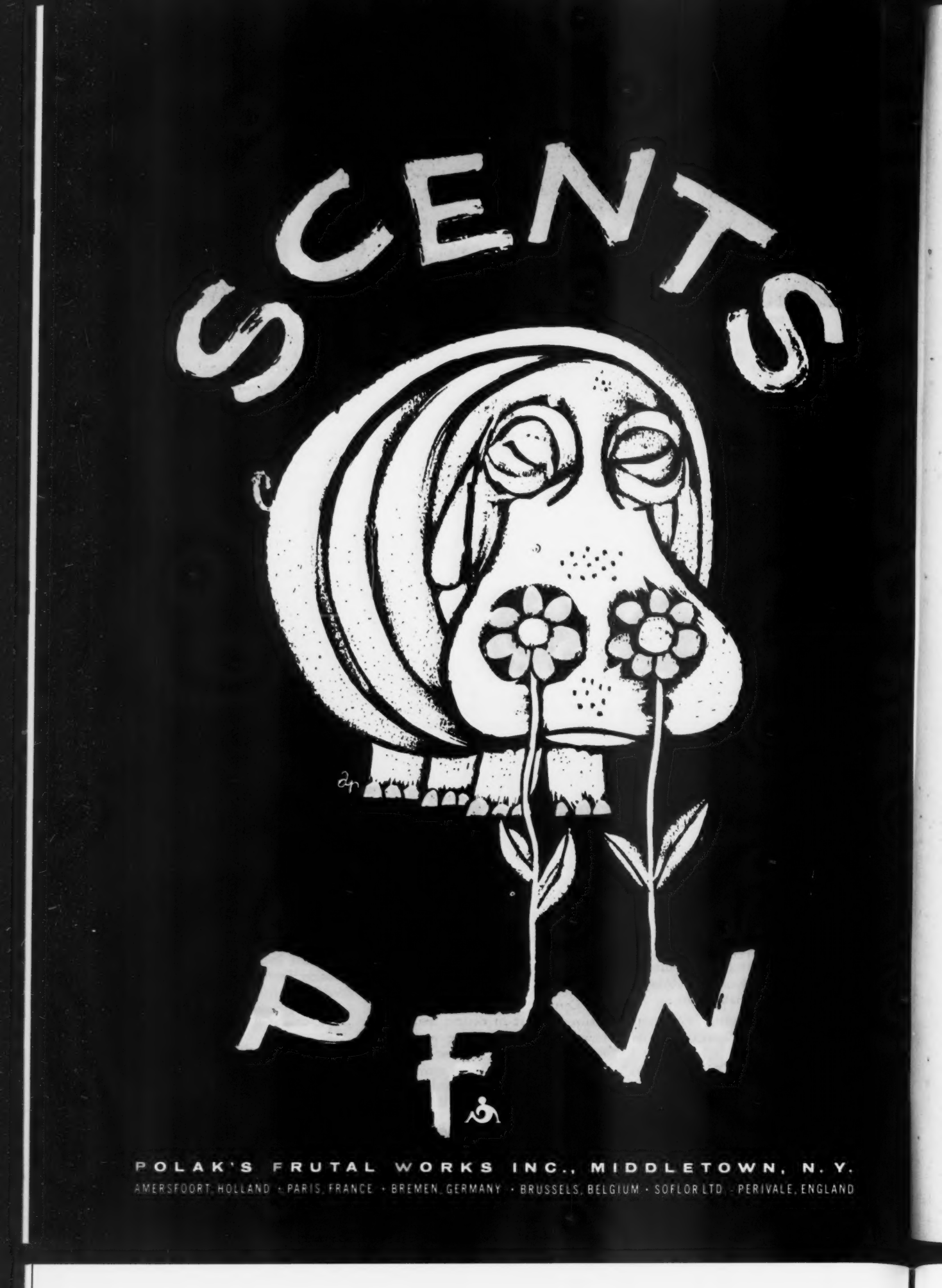
The following appointments have been made in the wholesale drug department of McKesson & Robbins, Inc.: **James W. Seibert,** vice-president in charge of buying; vice-president **Hugh S. Crosson,** with the company 20 years, transferred to the field buying department; and **Emmett E. Wilson,** drugs and proprietaries buyer.

The Squibb Institute for Medical Research has promoted **Dr. Miklos Bodanszky,** known for his contributions to peptide synthesis, to research supervisor, section of organic chemistry. **Dr. Leon J. Heuser,** who joined Squibb in 1946 and has worked largely in the field of antibiotics, is now research associate.

Revlon, Inc., has appointed **Robert Oppenheim,** previously with Clairol, Inc., director of marketing for hair color. Mr. Oppenheim joined Clairol in 1955 in a sales capacity.

A. S. Bedell has retired as treasurer of Beauty Counselors, Inc., after 29 years. Mr. Bedell continues as a member of the board of directors, and as a consultant.

Parke, Davis & Company has elected two new vice-presidents: **C. A. Erdmann,** with the company since 1951, as controller; and **Dr. George Rieveschl, Jr.,** with the company since 1943, as director of commercial development. **Winfred M. McElheny,** sales representative since 1956, has been appointed a field manager in the firm's Kansas City Branch. **Dr. William T. Ely** has joined the company as associate research chemist. Other Parke, Davis appointments include **Dr. H. E. Machamer,** assistant director of microbiological research; **Fred J. Champagne,** superintendent of production and engineering; **Dr. Bernard J. Sloan,** associate research microbiologist; and **Jean L. Juday,** assistant research biologist.



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HAROLD B. MARK

ROBERT H. CANNON, JR.

WALTER W. WELLER, JR.

ROBERT DAVIS

Verona Aromatics has appointed **Harold B. Mark** as sales representative for New Jersey and Pennsylvania.

Eastman Chemical Products, Inc., subsidiary of Eastman Kodak Company, has announced a number of changes in its organizational structure. **Robert H. Cannon, Jr.,** formerly regional sales manager, has been appointed assistant sales manager. **George J. Taylor,** formerly district sales manager, replaces Mr. Cannon as eastern regional sales manager. **W. C. Cooke,** formerly sales coordinator, replaces Mr. Taylor as district sales manager. **R. Clay Dubberly** and **David S. Oaks** have been assigned to the division's Cleveland office, with Mr. Dubberly as district sales manager. **C. R. Lee** has been made head of the Buffalo sales office, and **Ted K. Bailey** will represent Chicago.

Walter W. Weller, Jr., has been elected treasurer of Hoffman-La Roche, Inc. Mr. Weller joined the company in 1954 as assistant to the treasurer. **Milton J. Schiffrin, Ph.D.,** has been appointed director of clinical research in the medical research department. Dr. Schiffrin is co-author of Clinical Analgetics, editor of *Management of Pain in Cancer*, a contributor to *Physiologic Principles of Surgery*, and to medical journals. The Roche Laboratories Division has promoted **Thomas J. Tierney** to product marketing manager, from divisional sales manager, and has **Ross Cheney,** with the company since 1950, to western regional sales manager.

New Jersey Machine Corporation has appointed **Robert F. Davis, Jr.,** sales engineer, headquartered in the Chicago branch office. Mr. Davis will cover Illinois, Wisconsin, Minnesota, Missouri, and Kansas. He has been a member of the factory service department.

Dr. Gilbert F. Otto, previously head of the department of parasitology, has been appointed head of agricultural and veterinary research at Abbott Laboratories. Dr. Otto jointed Abbott in 1953 after holding a professorship at John Hopkins University. He has served as a consultant to various government departments, published numerous studies on parasitology, and was elected president of the American Society of Parasitology in 1956. Abbott has named **Tilden Batchelder, William M. Behrens,** and **Robert S. Frye** assistant directors of production.

Bruce K. Herbruck, formerly with Wallace Laboratories and Warner-Chilcott, has joined Maltbie Laboratories Division, Wallace & Tiernan Inc., as assistant to the medical director, Dr. Charles E. Hough.

Harold R. Almond, Jr., Ph.D., has been appointed a research chemist at McNeil Laboratories.

Mary Chandler, east coast department store supervisor, has been promoted to manager of department store sales, filling the position left by Marion McDonald's resignation.

William J. Flaherty, previously with Avon Products and Chesebrough-Pond's, has joined Imco Container Company, a Division of Rexall Drug and Chemical Company, as sales representative in New York City. **Tom Norwell** has joined the company as sales representative, in Montreal, Canada.

Elizabeth Carbide Die Company, Inc., has appointed **Laurence C. Johnston,** head of Johnston Engineering Sales Company, as sales representative for New England. **James V. Ray, Jr.,** and Associates will cover the New York City area.

Frank Pergolizzi, industrial chemist with Bristol Myers, has joined the Mennen Company as senior research chemist in the research and development department.

Henry Mahnken, with Onyx for 24 years, has been appointed chief control chemist, a new position at Onyx Chemical Corporation.

George H. Perbix, with Procter & Gamble Company since 1949, has been appointed to the newly created position of manager of the general buying department.

Benzol Products Company has appointed **Hal Bugbee,** formerly with United States Industrial Chemicals, as sales representative in the New York and New Jersey area.

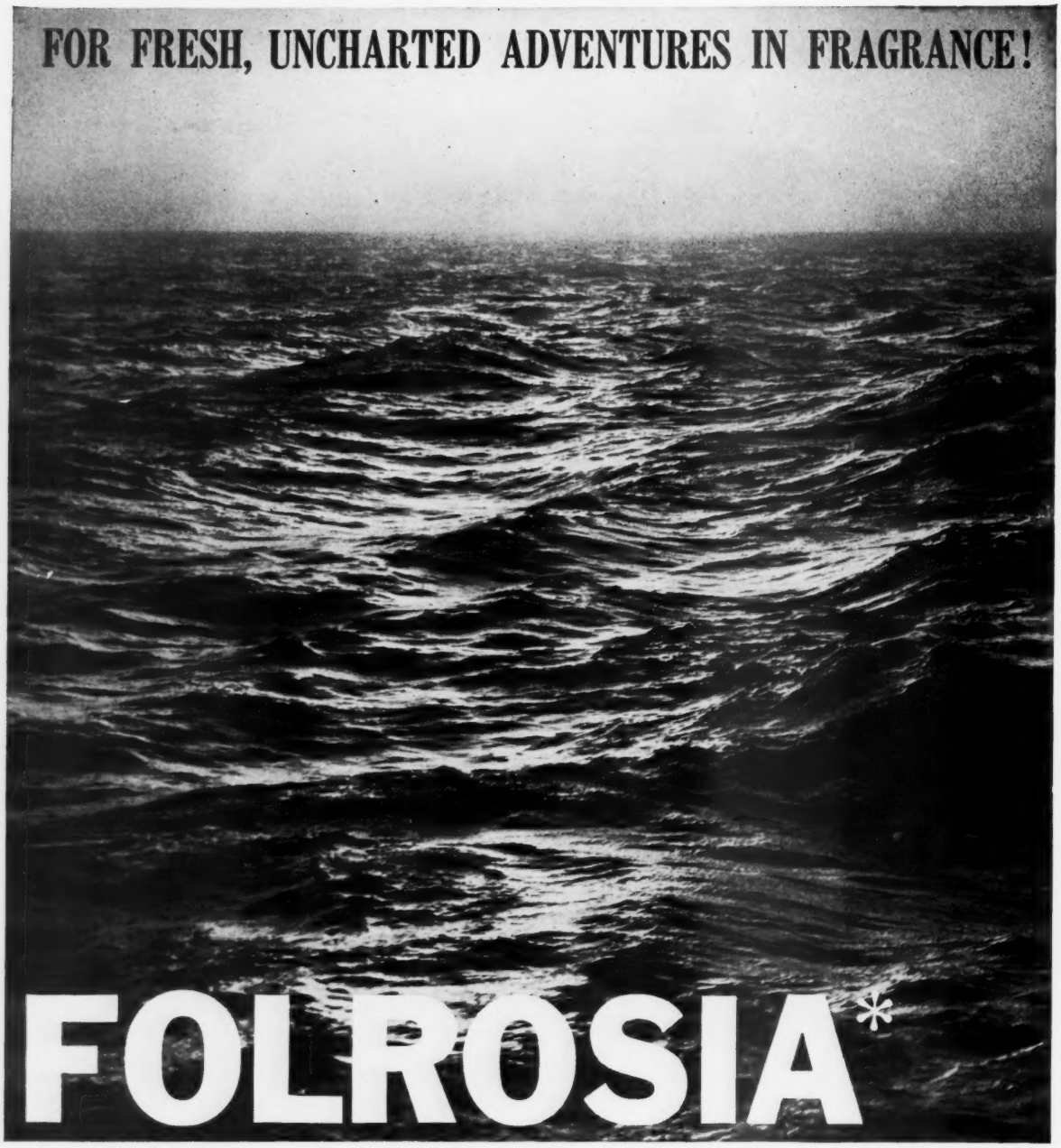
Becco Chemical Division of Food Machinery and Chemical Corporation has transferred **E. Michael McMahon,** sales representative in the Philadelphia area, to the northern New Jersey and eastern New York area, and has appointed **Sam L. Cassedy** to succeed him.

Jack Wilson, associated with the plastics industry for many years, has joined Augusta Plastics, Inc., in a sales capacity.

Jack Raymond, representitive of Consolidated Packaging Machinery Corporation, subsidiary of International Paper Company, in the Great Lakes area, has been assigned to the New York City office as assistant to Ed Baum. **Al Atkins,** who has represented the company in the Louisville area, will replace Mr. Raymond in the Great Lakes area.

Jeanne Richards, national home sales manager, has been promoted to manager of the franchising division, Dorothy Lamour, Inc.

FOR FRESH, UNCHARTED ADVENTURES IN FRAGRANCE!



...a new, "broad-spectrum" synthetic aromatic with a *deep red rose* character. Use it to create a crisp, natural, leafy rose aura . . . or to lend intensity and personality to subtler blends.

FOLROSIA blossoms with new levels of floral realism! Whether you wish to enhance familiar rose materials, create bold new rose accents of uncommon floralcy and naturalness, or add fresh, lifelike notes to more subtle compositions, FOLROSIA provides a simple, yet unusual answer.

FOLROSIA possesses remarkable tenacity, with a fragrance and nuances reminiscent of fresh green rose foliage. It is extraordinarily stable in soaps, detergents, cosmetic preparations, and its odor effectiveness remains at a high level over extended periods. Write for samples and technical data.

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GIVAUDAN

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New York 36, N.Y.

J & J President Retires

George F. Smith, president of Johnson & Johnson since 1943, and with the company since 1933, has retired.

Besides his work with the parent company, Mr. Smith has had a hand in establishing many of it's affiliates, notably, Permacel, Personal Products Corp., Ethicon, Inc., and Ortho Pharmaceutical Company.

Mr. Smith plans to continue a number of his other activities, among them, president of the National Fund for Graduate Nursing Education; director of the Health Information Foundation; a trustee of the National Fund for Medical Education; a director of the American Foundation for Pharmaceutical Education; and a member of the board of directors of the World Medical Association.

New P.I. Technical Director

James W. Field, formerly with the Technical Association of the Pulp and Paper Industry, has joined the staff of the Packaging Institute as technical and field service director.

Andrew A. Lynn Resigns

Andrew A. Lynn, vice-president and a director of Chesebrough-Pond's Inc., and president of the Prince Matchabelli division has resigned.

Mr. Lynn has been in charge of the company's domestic marketing.

Sickels Retires from P.D.

Ralph G. Sickels, an advertising-public relations executive for Parke, Davis & Company has retired after 40 years with the company. He continued for three years beyond retirement age, at the firm's request.

A.M.A. Drug Council Secretary

Dr. William C. Spring, Jr., has been appointed secretary of the American Medical Association's Council on Drugs. Prior to this appointment Dr. Spring has been medical director of the laboratories division of Chas. Pfizer & Co.

From 1952 to 1959, he held the DeLamar professorship, and headed the Division of Public Health Practice, School of Public Health and Administrative Medicine, College of Physicians and Surgeons, Columbia University, New York.

Hadley Retires from Lilly

Frederic M. Hadley, executive vice-president of Eli Lilly and Company since 1953, and with the company 32 years, has retired, to become vice-president of Wabash College in Crawfordsville, Indiana.

Among Mr. Hadley's new responsibilities will be the administration of the college's personal development program for young business executives and the direction of the college's ten-year program to enlarge its capital resources. Mr. Hadley has been active in the field of education as chairman of the Indiana Rhodes Scholarship selection committee, a trustee of Amherst College, and as a member of the board of directors of Butler University and the Earlham Foundation.

Balfour Phelan Retires

Balfour Phelan, vice-president of the Container Corporation of America, has retired after 25 years with the company. After serving in managerial positions, Mr. Phelan became vice-president in 1954, with responsibility for box board and carton operations, central division.

At the annual Christmas party of Givaudan-Delawanna, Inc., held at the Swiss Chalet, Rochelle Park, N. J., E. R. Durrer, president (center), presenting Swiss watches to 25-year staff members as Dr. M. Luthy, vice-president (left) observes. Members (left to right): M. Dombroski, A. Turow, C. Perra, A. Csupecz, and L. Balas. More than 300 employees attended the affair.

Commercial Solvents Manger Retires

Edward W. Bacigalupi, who has been with Commercial Solvents Corporation for 43 years, has retired as western regional manager. He will continue to serve as a special representative on the West Coast for the Sales Division on special projects.

EDWARD W. BACIGALUPI

Mr. Bacigalupi began with Western Industries Company in 1917, continued when it was merged with American Solvents and Chemical Company in 1926, and again, when the latter was purchased by Commercial Solvents in 1933.

McNeil Receives Procter Medal

Robert Lincoln McNeil, founder and retired president of McNeil Laboratories, has been named recipient of the Procter Medal, the achievement award of the Philadelphia Drug Exchange, "for his many years of leadership in the pharmaceutical industry."

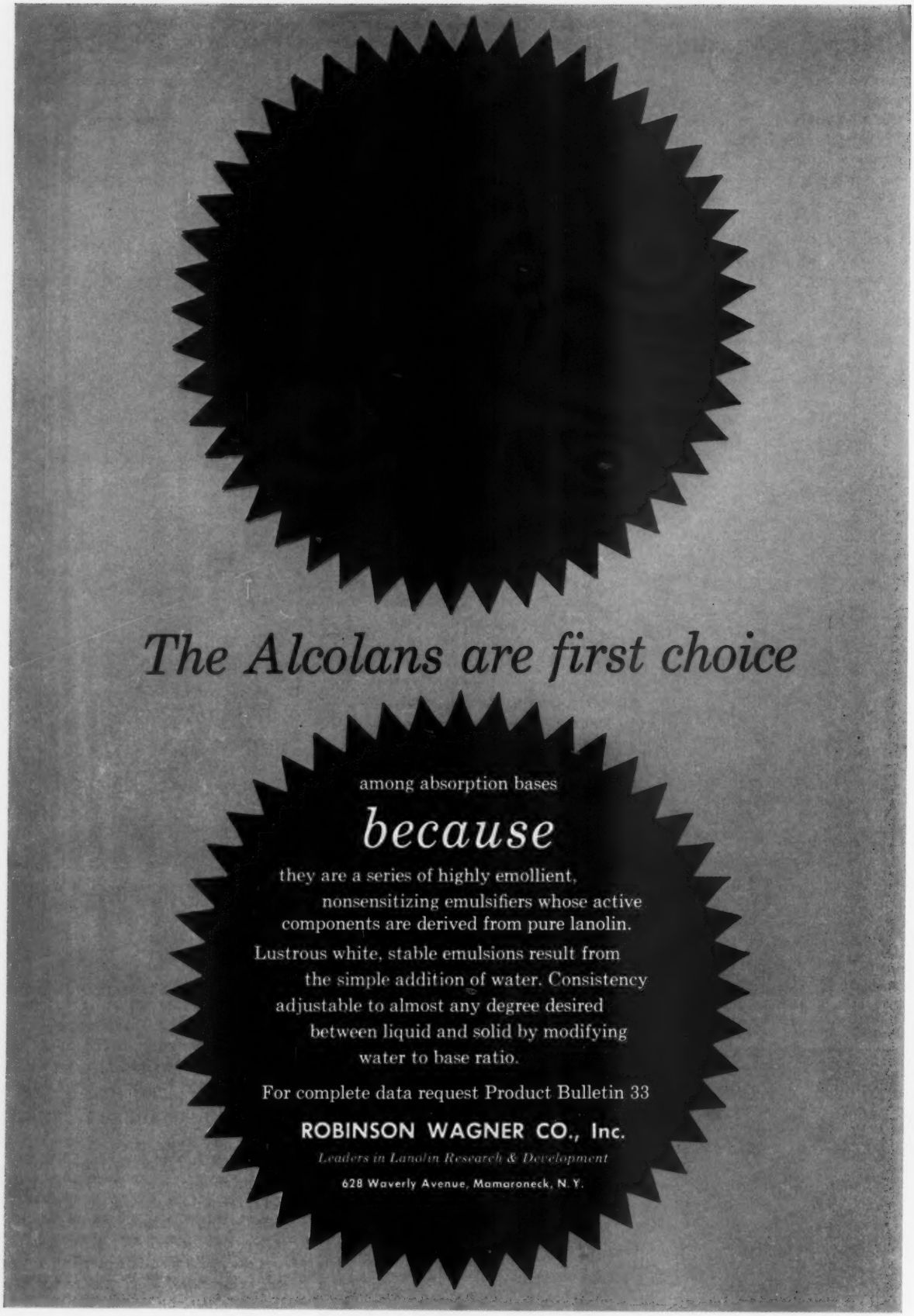
Formal presentation of the award was made at the annual dinner of the drug trade association on January 25, at the Bellevue-Stratford Hotel.

New Fritzsche Sales Award

Warren R. Godfrey was the winner of Fritzsche Brothers' new Salesman of the Year trophy to be awarded annually to the most deserving member of its sales staff. Mr. Godfrey has been with Fritzsche 25 years.

Top Breck Salesman

Francis E. Tierney, sales representative for John H. Breck, Inc., was recently selected, as the most outstanding salesman for 1960, to receive the Arthur W. Tosh Award, a heavy Chippendale sterling silver tray inscribed with the recipient's name, plus a sum of money.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they are a series of highly emollient, nonsensitizing emulsifiers whose active components are derived from pure lanolin.
Lustrous white, stable emulsions result from the simple addition of water. Consistency adjustable to almost any degree desired between liquid and solid by modifying water to base ratio.
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At the signing of the papers for the acquisition of Northam Warren by Chesebrough-Pond's, left to right: Northam Warren, founder and president until retirement in December 1960, Jerome A. Straka, president, Chesebrough-Pond's, and N. Warren, Jr., executive vice-president of the newly formed subsidiary.

Expansions, Acquisitions and New Plants

Chesebrough-Pond's Inc., has acquired the world-wide interests of Northam Warren Corporation, which will be operated as a wholly owned subsidiary. . . . **Smith Kline & French Laboratories** is purchasing Julian Laboratories, Inc. Under the planned acquisition, Dr. Percy L. Julian, founder and owner, will remain as president of Julian. . . . **Foster D. Snell, Inc.,** has acquired Calkin & Bayley, Inc. It will be operated as a wholly owned subsidiary, with George T. Bayley, C & B's former president and board chairman, acting as vice-president. Snell will soon close its Davis & Bennett Division at Worcester, Mass. . . . **Revlon, Inc.,** has purchased Zunino-Altman, Inc., which markets artificial plastic flowers, to be operated as a wholly owned subsidiary with no changes contemplated in personnel or policies. The purchase was for cash, and no Revlon stock was involved. Other financial details of the transaction were not announced. . . . **Mary Chess, Inc.,** has purchased the world-wide rights of Parfums Lucien LeLong, Inc., with branches in Paris, London, and Montreal. It will be operated as a wholly owned subsidiary. . . . **American Hospital Supply Corporation** has announced negotiations for an exchange of American stock for all shares of Midwest Dental Manufacturing Company. . . . **Sterling Drug Inc.** has announced the formation of Breon Laboratories Inc. as a new pharmaceutical subsidiary. Comprised of four divisions, Breon Rx Division, American Ferment Division, Diaparene Division, and Esta Medical Laboratories, the new Breon subsidiary will take over the marketing of the products of all four Sterling pharmaceutical units. Charles L. Czermak, president of George A. Breon & Company since January 1960, is president of the new subsidiary; Charles C. Wood, vice-president, sales, American Ferment, is vice-president, sales; and Dr. Ross V. Sayers is vice-president and medical director, the same position he had held with George A. Breon. . . . **McKesson & Robbins, Inc.** plans to open a new drug division in Everett, Wash., and one in Culver City, Calif. . . . **Sun-Lac, Inc.,** has opened a new aerosol custom loading plant with increased filling capacity and warehouse space, and expanded shipping facilities, at Industrial Park, N. J. . . . **The Lord Baltimore Press,** a subsidiary of International Paper Company, has opened sales offices in Cleveland to serve northern Ohio, eastern Michigan and western Pennsylvania. . . . **United States Testing Company** has appointed the Arthur Colton Company as exclusive sales representative in the continental United States, for its ACCEP-TRON Inspection Instrument. . . . The eastern district sales office of **Du Pont Company's** Freon Products Division is moving to new quarters in East Orange, N. J., with larger and more modern office space in a location reached easily by car. . . . **Du Pont Dyes and Chemical Division** is transfering its New York district sales office, laboratory, and warehouse to Clifton, N. J., to improve service to customers in New York State and northern New Jersey. . . . **White Metal Manufacturing Company** has announced the addition of a new rotary casting installation for the production of aluminum slugs. Completion of the new facility climaxes a program of international cooperation, between White Metal, an independent aluminum fabricator, and its principal supplier of primary aluminum ingot, Aluminium Limited of Canada.

McKnight of Lueders Retires

James McKnight, salesman for George Lueders & Co., Inc., New York, has retired after 53 years of uninterrupted traveling for the company, not only in New York, but also in Ohio, Michigan, Pennsylvania, and Indiana.

Essential Oil Assoc. Head

R. E. Horsey, vice-president of sales at Givaudan-Delawanna, Inc., has been named to a second consecutive term as president of the Essential Oil Association.

Award Nominations Invited

Dr. C. O. Willits, president of the Association of Official Agricultural Chemists, has announced that nominations are now being accepted for the fifth AJAC Harvey W. Wiley Award for Achievement in Analytical Methods. This award of $500 will be given to the scientist or group of scientists who have made outstanding contributions to the development of analytical methods for foods, drugs, cosmetics, feeds, fertilizers, and pesticides for use in general analytical chemistry.

Nominations must be submitted by April 1, 1961, to the secretary, William Horwitz, Box 540, Benjamin Franklin Station, Washington 4, D. C.

Snapped during a visit of Dr. Robert Henry Marriott (center), director of products research at County Laboratories, Ltd., Great Britain, and SCC award winner, to Old Empire Inc. research and development laboratories. Left to right: E. N. Reyner, teachnical director, Old Empire; John D. Horn; Dr. Marriott; Claude S. Welton; and John De Elorza, president of Old Empire.

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GLYCOL AND POLYGLYCOL ESTERS

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Synthetic Wax with Melting Point of 140°-143°C. (284°-290°F.)

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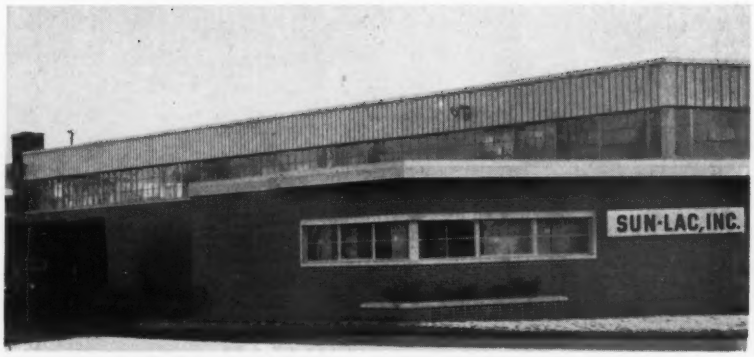

New and larger aerosol custom loading plant opened by Sun-Lac, Inc., at Industrial Park, N. J.

Chicago Association Elects Officers

The new officers of the Chicago Drug and Chemical Association are: president—S. A. Davis, president of C. P. Hall Co.; first vice-president—Robert DeLamar, J. H. DeLamar and Sons, Inc.; second vice-president—J. C. Browning, Demert and Dougherty; secretary—Kenneth W. Hartley, Dodge & Olcott, Inc.; and treasurer—Walter L. Johnson, Fairmount Glass Works, Inc.

Risdon Is 50 Years Old

The Risdon Manufacturing Company has just published "Connecticut Enterprise," a book telling its corporate and community story, to commemorate the firm's 50th anniversary.

Its 104 pages describe the company's beginnings in 1910, when 114 Connecticut citizens jointly purchased an almost bankrupt toolworks, and its progress to the present.

Schering Sponsors Symposium

The University of California Medical Center presented a three-day symposium, entitled "Man and Civilization: Control of the Mind," in San Francisco during January. Sponsored by the Schering Foundation, which was established and is supported by the Schering Corporation, it focused on the factors controlling the mind and their interactions.

BIMS Annual Banquet

The BIMS annual banquet was held on February ninth at the St. Regis Hotel in New York City. An exceutive committee including Peter L. Forsman, C. H. Forsman Co.; C. R. Keeley, *Beauty Fashion;* E. J. Moore, Richford Corp.; and Leonard H. Schultes, The Hewitt Soap Co., Inc., has been selected.

Perfumers Meet in April

At the seventh open annual symposium of the American Society of Perfumers, Inc. to be held on April 13, at 2:00, at the Essex House, Central Park South, N. Y. C., three speakers will discuss the theme "Experimental Findings on Odor and Olfaction." Dr. Trygge E n g e n, Brown University, will speak on cross-adaptation effects, changes in thresholds after exposure of subjects to different odors, as well as the identification capacities of untrained observers; Dr. D. Tucker, Florida State University, will discuss the olfactory process, studies on the receptor mechanism, and the process of odor discrimination; and Dr. M. G. Beets, International Flavors and Fragrances, Inc., Hilversum, Holland, will discuss the relationship of odor and molecular constitution.

The meeting will be followed by cocktails and a buffet supper. Reservations can be made through Edwin D. Morgan, Jr., Lever Bros. Research Center, 45 River Road, Edgewater, N. J.

TV Health Programs Continue

The program of television lectures by members of the faculty of the Philadelphia College of Pharmacy and Science broadcast through the University of the Air facilities of WFIL-TV, Channel 6, in Philadelphia, is to continue through the second semester, February 10 to May 26, inclusive. These presentations will be m a d e on Friday mornings, from 11:15 to 11:35 o'clock.

As in the past, the general theme is "You and Your Health," but each of the several topics will be new. Registrar John E. Kramer is host for the entire series.

L. J. Woolf

Louis J. Woolf, chairman of the board of directors of H. Kohnstamm & Co., Inc., died in New York City on January 12, 1961. Mr. Woolf was 70 years old.

Mr. Woolf spent 47 years with Kohnstamm, beginning in 1914. He was soon appointed sales representative in the color and flavor divisions, and thereafter held increasingly important positions, until becoming president in 1950, and chairman of the board in 1957.

During his career, Mr. Woolf acquired recognition for his knowledge of such specialties as carbon paper and printing ink, and served on several committees connecting with the welfare of the printing ink industries. He was also active in many trade associations, among them the Flavoring Extract Manufacturers Association and the Fruit and Syrup Manufacturers Association. He was at one time president of the Dry Color Manufacturers Association.

H. W. Ambruster

Howard W. Ambruster, who spent a lifetime fighting for the strict enforcement of pure food and drug laws, and against the international chemical trusts, died on January 10, at the age of 82.

Mr. Ambruster was a chemical engineer, writer, and lecturer. In one of his books, "Treason's Peace," Mr. Ambruster traced the operations of the German dye companies in relation to the United States, prior to World War I.

I. Colbert

Irving Colbert, director of the Products Application Laboratory of the Malmstrom Chemical Corporation died January 7. He was 47.

Mr. Colbert had been membership chairman of the N. Y. Chapter of Cosmetic Chemists for the past three years. Before joining Malmstrom in 1956, he had been cosmetic chemist with Revlon, and later with Coty, and was assistant director of research for Block Drug Company.

W. Dugan

Walter Dugan, vice-president and general manager of Welch, Holme & Clark Co., Inc., died on January 3 of a heart attack.

An expert on warehousing, Mr. Duggan had become general manager in November of 1960.

Wyeth Boosts Equanil Tablet Production from 600 TPM to 3200 TPM—Quadruples Slugging Speed with Colton Presses and I. D. F.*

Wyeth Inc. reports a dramatic example of how Colton Tablet Presses with Induced Die Feed boost tablet production.

Wyeth first used induced die feeding with an older Colton press with 27 stations tableting Equanil from granulations at 600 TPM.

When this press was equipped with Colton Induced Die Feed Attachment, production jumped to 1500 TPM, an increase of 150%.

Wyeth then switched Equanil production to a new Colton Double Rotary Tablet Press No. 241 with 41 stations and production skyrocketed to 3200 TPM, an increase of 430% over the original 600 TPM.

In addition, a Colton No. 240 Single Rotary Slugging Press with 16 stations and Colton Induced Die Feed Attachment was installed for slugging Polymagma, Streptomagma with Attapulgite, Purodigin, Meprobamate, and Darcil and all are now being slugged at four times the speed possible with previous equipment.

Although slugging is involved in all of these operations, Colton Induced Die Feed is frequently used in tableting direct from powders and not only turns in some spectacular production records but also delivers tablets with all the desired accuracy in weight and dimension plus superior hardness and elegance and fast disintegration.

These benefits are available to you at a fraction of the cost of installing equivalent capacity conventional machines. Why not write us?

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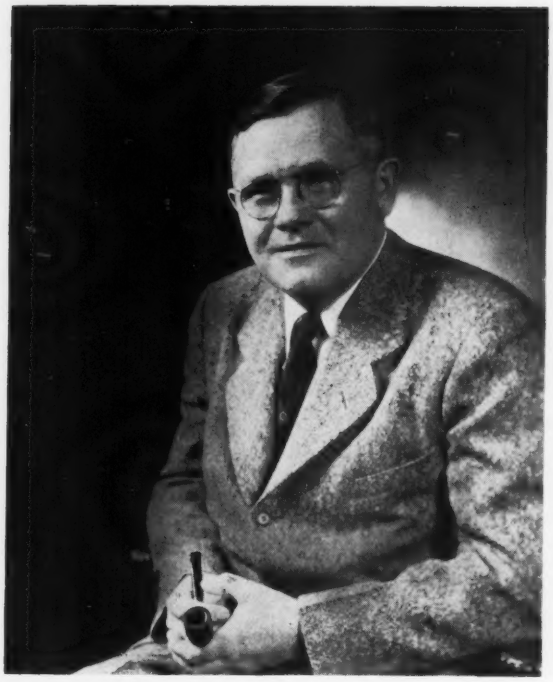


Management Forum

BY FRANCIS CHILSON, Sc.D.
PROFESSIONAL ENGINEER

Development Responsibility

Who should be responsible for product and process development—the research department? the production department? Should it be independent, reporting to the executive vice-president?

I participated in an argument about this one recently. Some development men feel that they should not only dictate a process but they should dictate the production equipment employed in manufacture. Production men and engineers are loath to accept mandates thrust upon them by R&D. They say the long-haired baboons in R&D don't know anything about production and, in any case, the production department should not be asked to take responsibility for the operation of equipment in the selection of which production people have had no voice.

Some of the most inefficient and cumberson manufacturing methods I have ever seen were dictated by R&D people. I inspected several of the largest tablet manufacturing plants in the U. S. recently and, one and all, they were deplorable because manufacturing methods had been laid down by R&D, supported by management. This problem gets into marketing. Once a product becomes successful, the marketing people shiver in their boots at the very thought of a product change, even when the change does not affect the color, taste, texture, appearance, size or any other discernible feature of the product. I remember once changing a batch size from 200 pounds to half a ton. Coincidentally, sales of this product fell off about 15 per cent below the quota for the period. The marketing people screamed bloody murder! The plant manager and I had ruined the business! A couple of months later, sales shot up about 30 per cent above quota, and once again the sun shone upon us.

In the good old days in the trade, all R&D work was done in the factories, more often than not by production people themselves. This was especially true in tablet development. Then research as a separate function came along, and with it the need for some sort of pilot plant to scale up batch size from lab bench to a close approximation of plant equipment capacity. Separate pilot plants became necessary because of the rows between production people and research people over the use of production equipment. Many a battle I had to referee on this one!

As research developed, particularly in the synthetic organic field, still another type of pilot plant became necessary, to scale up syntheses that could be made on the bench but might not be amenable to larger operation. So, in the course of time, the larger organizations had two pilot plants, one for organic synthesis and the other for pharmaceutical formulation.

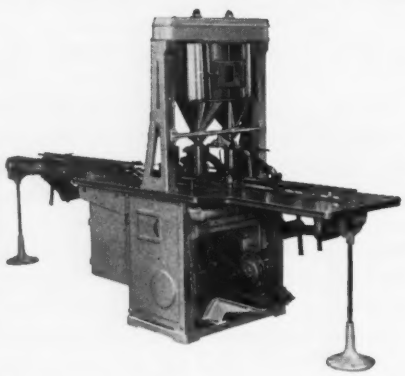
There is no question in my mind but that, in a pharmaceutical factory, the chemical pilot plant, even though it is operated—as it should be—by a chemical engineer, should be responsible to the research department. Since more compounds go into such a pilot plant than ever emerge from it, such a plant is a working tool of the research department.

I think also that the pharmaceutical pilot plant or development department should be under the jurisdiction of the research department. It is concerned with converting research products into acceptable working formulas and dosage forms. As a rule, this department makes all clinical trial requirements. The product never becomes an immediate concern of the production department until the clinical trials have proved it out, although the production department should be notified as soon as the clinical trials appear to be successful.

When a product has been proved clinically, it becomes necessary to write a working formula for making it and to set up the necessary controls. At this point, the cooperation of development, control, and production is needed. Similarly, when the first few

FMC Auger Fillers meet high-quality standards for Chesebrough-Pond's

Chesebrough-Pond's Inc., has long been well-known in the cosmetic industry for products of the highest quality. For many years they have used FMC Auger Fillers to meet the high standards they maintain for their powder and talc products. Ten FMC automatic and semi-automatic fillers of three different types fill a wide variety of sizes and kinds of containers from gold-finished metal canisters to lithographed paperboard drums.



The Duplex Auger Filler model HG-84 is one of the FMC units installed at the Chesebrough-Pond's plant in Clinton, Connecticut. Completely automatic, this model is designed with a choice of filling methods—cam volumetric, gross weighing, or auger combined with vacuum for pack filling dusty products—at speeds up to 70 containers per minute. Many other models are available for large or small plants, automatic or semi-automatic operation, tight or loose fills, long or short runs to handle powders, granules, and certain pastes. Production run accuracy has proved outstanding in filling cans, jars, boxes, bags, etc. from ½ oz. to 20 lb. Changeover for product and size is exceptionally fast and simple. Speeds as high as 140 per minute.

Putting Ideas to Work

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For the whole story of how FMC Auger Fillers can improve your packaging, write for Bulletin P-811.

production runs are made, the cooperation of R&D is required to make certain that the mass-produced product conforms to all requirements. Where equipment is not available for the manufacture of a new product, the production and engineering department should have the final word in regard to equipment selection or design. I think also that the production department should be given the opportunity by R&D to criticize all working formulas before they become official. As a rule, production men have had far more experience in manufacturing methods and equipment than R&D men, and should be able to suggest the best possible way of making new products. While I am firmly of the opinion that production should never be permitted to alter a manufacturing process without the approval of R&D, no process should ever be regarded as final and perfect and no limitation should be placed upon the plant manager's right to suggest changes when, in his opinion, economies and other improvements will result. But he should be obligated to prove his case to R&D. I have witnessed too much trouble from changes made in factories without proper authorization. Let's be rigid as to requiremnts, but flexible as to approach.

Red Tape

It is characteristic of almost every organization that, while it is buried in records, it has no information, certainly not adequate management information. It has always seemed to me that one of the duties of a controller was to control the spawning of useless records. Let me bite off now a little chunk whereby millions could be saved without harming anyone. I refer to quarterly reports, dividend checks, proxy notices, dividend tax notices and the like. A dividend check properly designed could be made to serve also as quarterly financial report, a proxy statement, a tax summary. The check need only be twice as long as it is, with a center perforation. Some companies send me three documents every quarter in a single envelope, with a first-class stamp on it; others —silly asses—send me two and sometime three mailings—all first-class—every quarter. Some will send a preliminary notice that a dividend has been declared and will be paid as of a certain date. Let's have more dividends and less paper.

Socialized Medicine

Call it what you like, but I am all for it. As I have said here before, socialized medicine is working very well in England. Doctors and pharmaceutical manufacturers alike are making more money than they ever did before its inception, in spite of what we would regard as onerous restrictions. In this country, doctors are so busy making money that they have no time for their patients, and I for one, am damned tired of having to go through the hands of five or six specialists to discover the reason for a simple ailment —only to find, as it turned out recently, that they all were wrong. One attributed my condition to a liver ailment; another to my kidneys; a third to nerves; and a fourth to stomach. Finally, I went to a friend of mine, whom many of you know, an MD who was, before he studied medicine, an electrical engineer. I knew he'd take time to study my case and that he'd know how to think straight. He found out in a short time what actually was wrong. If mine were an isolated case, I'd not complain. But I've had several similar experiences before. So has my wife. So have all my friends. Criticism of doctors is universal. Many of them have no time for anything except your money. They are not thorough. They are not competent.

Hospitals are not to be exempted from criticism. Charges are exorbitant, and yet they seldom break even because of mis-management. Nowadays they demand a financial statement before a patient is admitted. A friend of mine was asked to pay $350.00 in advance before a well-known hospital would admit his sister. My wife recently paid a hospital bill of $475.00 for four days of disgraceful treatment in a well-known New York hospital—this bill, incidentally, did not include the salaries of private nurses. And my wife should know something about hospitals; she is an RN and once was superintendent of a small hospital herself.

We regulate the charges of telephone companies, of gas and power companies; we regulate the rates of railroads; we scrutinize banks on a continuing basis—why shouldn't we regulate the rates charged by doctors and hospitals? Why shouldn't we scrutinize their work continuously, as they do in England? The A.M.A. runs a tightly closed union but does nothing to protect the public against incompetent medical practitioners. To the A.M.A. I say "Mene! Mene! Tekel! Upharsin!

Ideas To Ponder

"Our slow world," wrote Woodrow Wilson in 1890, "spends its time catching up with the ideas of its best minds. It would seem that in almost every generation men are born who embody the projected consciousness of their time and people.

"Their thought runs forward apace into the regions whither the race is advancing, but where it will not for many a weary day arrive . . . the new thoughts of one age are the common-places of the next. . . .

"The men who act stand nearer to the mass than the men who write; and it is in their hands that new thought gets its translation into the crude language of deeds. . . ."

It cannot be said that the men of ideas of the country have failed to perform their traditional tasks in these last few years. They have observed the convulsions of our time and let their minds run ahead to the logical consequences for the nation.

I cannot remember a time when there has been more purposeful thought on contemporary problems

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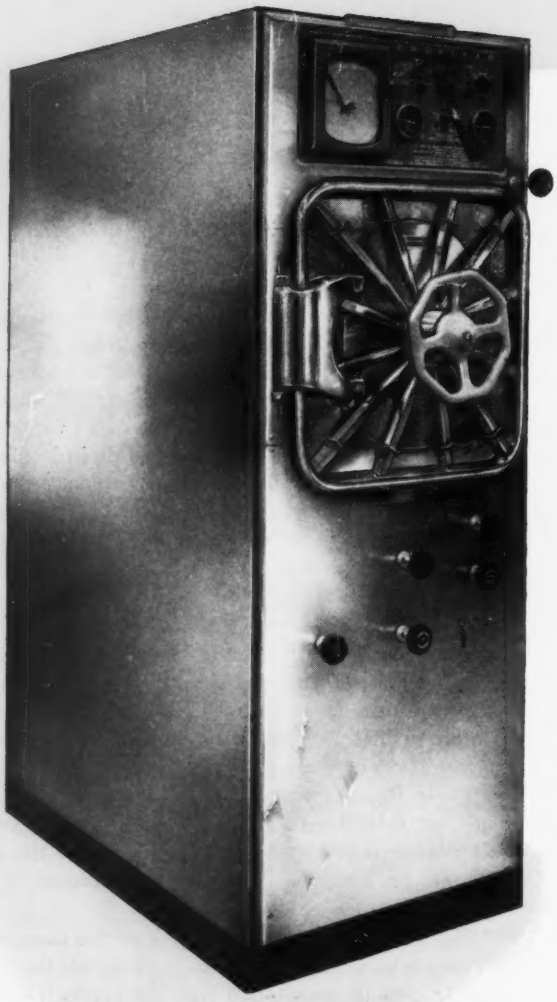

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The fully automatic Cyclomatic Control assures positive standardization of techniques with a minimum of time and attention from the operator.

Up to 100% greater usable capacity is provided by the square chamber which permits more efficient loading. Installation and maintenance are simpler and less costly because of the stainless steel cabinet.

For steam or electric heat. Chamber sizes 16″x 16″x 24″ or 20″x 20″x 36″.

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in the universities and foundations than now. Their reports and conclusions would fill a good-sized library, but the alliance between them and the White House has been feeble, and somehow it must be restored.

The problem is not that the Soviet Union produces better engineers than the United States—though it certainly produces more—but that it can direct its engineers into these new countries or anywhere else that helps promote the purpose of the state.

As Dean McGeorge Bundy of Harvard has pointed out:

"It may be that we are at the edge of a time in which authoritarian societies, controlling and using this new investment, the human mind, will be able to produce revolutions in power and in growth as remarkable to us as our own revolution, the industrial and technological revolution of the last 150 years, is remarkable today to the people who inhabit the world of rising expectations."

According to James Reston of *The New York Times:*

"To me, this hazardous possibility that centralized control of technology and of science behind it may lead to a new order of growth, of power, and of change in the hands of people with a high degree of political purpose and centralized and ruthless control, seems to be the real danger in the growth of Soviet and Chinese power."

The Scholar and the Research Scientist

The following exerpts were taken from a talk given to the 1960 Freshman Class at Yale University by Dr. Edmund S. Morton of Yale. I wonder how many of them knew what he was talking about?

"The world does not much like curiosity. The world says that curiosity killed a cat. The world dismisses curiosity by calling it idle, or *mere* idle, curiosity—even though curious persons are seldom idle. Parents do their best to extinguish curiosity in their children, because it makes life difficult to be faced every day with a string of unanswerable questions about what makes fire hot or why grass grows, or to have to halt Junior's investigations before they end in explosion and sudden death. . . . . Within the University they go on asking their questions and trying to find the answers. In the eyes of a scholar that is mainly what a University is for. It is a place where the world's hostility to curiosity can be defied . . . .

"All this does not mean that the answers which scholars find to their questions have no consequences. They may have enormous consequences; they may completely alter the character of human life. But the consequences seldom form the reason for asking the questions or pursuing the answers. It is true that scholars can be put to work answering questions for the sake of the consequences, as thousands are working now, for example, in search of a cure for cancer. But this is not the primary function of the scholar. For the scholar the consequences are usually incidental to the satisfaction of curiosity. Even for the medical scholar, the desire to stamp out a dreaded disease may be a less powerful motive than the desire to find out about the nature of living matter. Similarly, Einstein did not wish to create an atomic bomb or to harness atomic energy. He simply wanted to find out about energy and matter . . . .

"Since so many respectable people assure us that they have found the truth, it does not sound like a dangerous thing to look for. But it is. The search for it has again and again overturned institutions and beliefs of long standing, in science, in religion, and in politics. It is easy enough to see today that these past revolutions brought great benefits to mankind. It was less easy to see the benefits while the revolutions were taking place, especially if you happened to be quite satisfied with things the way they were before. Similarly it is not always easy today to see that the satisfaction of a scholar's curiosity is worth the disruption of society that may result from it. The search for truth is, and always has been, a subversive activity. And scholars have learned that they cannot engage in it without an occasional fight . . . .

"A second quality that makes a scholar has no apparent relation to the first and yet is inseparably connected to it. It is a compulsion to communicate. A scholar is driven by a force as strong as his curiosity, that compels him to tell the world things he has learned. He connot rest with learning something: he has to tell about it. Scholarship begins in curiosity, but it ends in communication And though scholars may in a university take refuge from the world, they also acknowledge responsibility to the world, the responsibility to communicate freely and fully everything that they discover within the walls of their sanctuary. The search for truth needs no justification, and when a man thinks he has found any part of it, he cannot and ought not to be silent. The world may sometimes not care to listen, but the scholar must keep telling it until he has succeeded in communicating . . . .

"Communication is not merely the desire and the responsibility of the scholar; it is his discipline, the proving ground where he tests his findings against criticism. Without communication his pursuit of truth withers into eccentricity. He necessarily spends much of his time alone, in the library or the laboratory, looking for the answers to his questions. But he needs to be rubbing constantly against other minds. He needs to be tested, probed, and pushed around. He needs to be made to explain himself. Only when he has expressed himself, only when he has communicated his thoughts, can he be sure that he is thinking clearly."

Taps

Dr. Irvine W. Grote, the peregrinating professor from Chattanooga who travels every summer from Hell to Breakfast, told me a story that must no longer go unpublished. It really is not Irvine's story; it is

NEW PRECISION IN MULTI-LAYER TABLETTING:

now you can check weight and analysis

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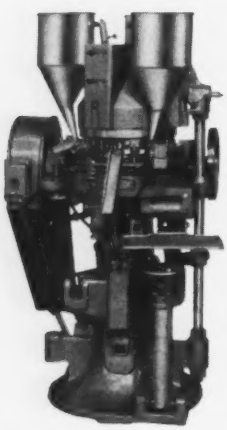
By pre-compressing each layer, Stokes achieves a well-defined surface of separation between each tablet layer. There's no intermixing of separate granulations . . . no loss of bonding qualities.



Stokes has created a new era in multi-layer tabletting! Now you can get the same degree of quality control in your multi-layer tablets as you have been getting in single layer tablets.

First in precision, control . . . The newly patented *pre-compression* and *manual ejection* features of Stokes Model 566 and 563 Multi-Layer Tabletting Presses eliminate the inaccuracies of conventional single compression techniques. *By pre-compressing each layer,* Stokes presses permit accurate weight and analysis control with precise, fine line separation of layers. The *manual ejection* feature lets the operator check pre-compressed layers for weight and analysis at any time . . . even when the machine is running at full production speed.

First in versatility, economy . . . Only Stokes presses give precision of special purpose design with versatility of all-around tabletting production. Model 566 can be used to press single-, two-, or three-layer tablets without changing cams, feed frames, hoppers, etc. Model 563 makes an excellent one or two layer tabletting press . . . and both presses can be used for conventional tabletting. Presses are designed to accept standard Stokes BB-2 tools . . . permitting maximum economy through utilizing existing dies and punches . . . easy, inexpensive tool changeover.

For complete technical data on these multi-layer tabletting presses, write for Data Sheet 106. Be sure to consult Stokes Engineering Advisory Service for complete technical assistance in designing parts, punches and dies, or complete production facilities.

STOKES

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his sister Merle's. For many years, Merle lived in the Tennessee mountains 20-odd miles from Chattanooga. She had lived there for so many years because the high altitude semed to be beneficial for her arthritis. She lived there so long, in fact, that all the hillbillys round-about trusted her completely. Shortly after the Korean War, Merle was invited to attend a military funeral for one of the local boys who had been killed in Korea. Surviving the soldier were his mother and his five-year-old son. Merle went along to the cemetery, mainly because she had never witnessed a military funeral before. A bugler blew taps and at the appropriate moment the honor guard lined up before the grave and fired a volley that reverberated through the wooded hills. Evidently the little old lady, the soldier's mother, had not expected the soldiers actually to fire their rifles, for she fell into a dead faint, and, at that moment, the little boy shouted excitedly, "Goddamn! They done shot Granmaw!"

Threaded Glass Needle Valve

Glass Products Division, Fischer & Porter Co., Warminster, Penna., has devised a threaded glass and Teflon needle valve that provides fine fluid control and permits continuous observation of flow. The tube is threaded by an exclusive process that eliminates need for conventional metal threads and allows for simplified two-piece construction. The wetted tip of the glass needle is of chemically inert Teflon, which will not corrode or leak; the needle valve stem, which is made of Kel-F, is sealed with a "Viton A" o-ring. The valve has a maximum orifice of 0.05 inch and has been used successfully with applications down to 10^{-6} mm of mercury.

Temperature and Humidity Controller

American SF Products, Inc., 420 Lexington Ave., New York City has developed a small and self-contained unit, designated KDEB 10, that provides a complete facility for automatically regulating temperature and humidity with extreme accuracy in areas up to 2500 square feet. It is intended for use in constant humidity rooms and other environmental testing facilities. The unit is 41 inches long by 34 inches high and 27 inches deep.

New Model Dissolver

Morehouse Cowles, Inc., 1150 San Fernando Road, Los Angeles 65, Calif. has specially designed and engineered a new dissolver, Model 515-VHV, for low to medium volume production requirements.

Applicable to a wide variety of chemicals, paints, inks, foods and similar products the 515-VHV is a high-speed, high-shear, impeller-type unit. It is capable of mixing, dispersing, deagglomerating, etc., materials up to 50,000 centipoises or more, and is powered with 10-15 h.p. motor, handling 50 to 200 gallon batches, depending on the nature of product and processing required.

Filter Aid

Johns-Manville Corp., 22 East 40th St., New York 16, N. Y., has developed a diatomite filter aid, called Celite 560, having a flow rate nearly double that of the fastest available filter aid materials. Celite 560 is shipped in 50-pound bags.

New Machine Press

Oliver Machinery Company, Grand Rapids, Michigan, is manufacturing a new Imprinter-Rewinder machine, No. 900. Label imprinting is the basic function of the machine, but it also provides a rewind operation, following imprinting, for labels that are to be kept in rolled form.

Label Printer

Faymus Div., Bankers & Merchants, Inc., 4410 N. Ravenswood Ave., Chicago 40, Ill., has developed a label printer that automatically prints, codes and prices on rolls in any quantity of pressure-sensitive labels.

Gallon Twin Filler

Elgin Manufacturing Company, 200 Brook St., Elgin, Ill., has introduced a new, high-speed production Gallon Twin Filler for a wide range of viscous and semi-viscous products. The new filler simultaneously delivers accurate filling to two glass, tin or aluminum containers from pints to gallon sizes.

Process Filter

Gelman Instrument Company, Chelsea, Michigan, has developed a new process filter for filtering submicron particles from liquids. The filter unit is based on the use of a porous plastic sheet with uniform submicron holes in it. The sponge-like cavity arrangement acts as a sieve to trap all particles of 0.1 micron and above in the filter.

Pedestal-type Sifter

Sprout, Waldron & Company, Inc., 130 Logan St., Muncy, Pa. has developed a new pedestal-type sifter to meet the sanitary specifications of the food industry and processing industry for a unit with quick cleaning advantages.

The split, special-spun stainless steel circular sifting bowl, 18 inches in diameter, can be quickly taken apart by release of the special clamping device. This exposes the circular screen frame, that can be lifted out. The screen cloth is attached to a stainless steel screen frame with food quality solder. There are no ledges, cracks or crevices to cause contamination. The screen area is 1.4 sq. feet and is activated by a ¼ h.p. motor. It is recommended for small and medium capacity, where overs do not exceed 5 per cent of input.

20-Quart Cooker/Mixer

Groen Manufacturing Co., 1900 Pratt Boulevard, Elk Grove Village, Ill. has introduced a new twenty-quart model TDC/TA-20 cooker/mixer as an addi-

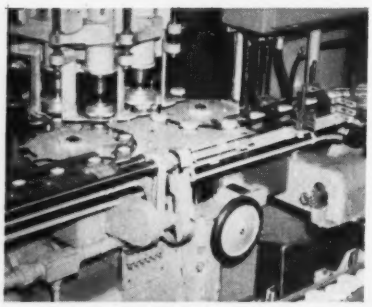
Famous remedy continues to thrive *Advertisement*

NOXZEMA KEEPS PACE WITH MODERN METHODS

- Up-to-date merchandising and machinery feature success
- Pneumatic equipment plays important role

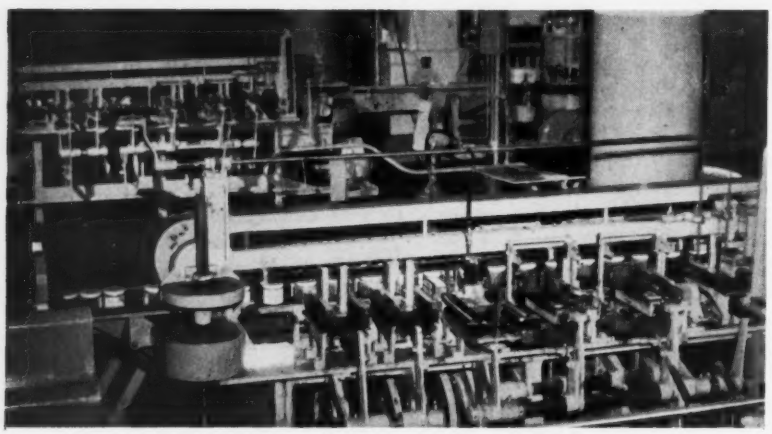
Born in a back room of a Baltimore pharmacy in 1914, Noxzema has grown in stature so that today, to millions of Americans it is a symbol of skin care and skin comfort. Highly competent, imaginative merchandising and the maintenance of maximum manufacturing efficiency through the use of up-to-date machinery have helped keep Noxzema a front runner in its field for over 35 years.

Noxzema's packaging facilities are a notable example of the company's progressive type of operation. In readying the Noxzema jar for market the knurled, turn-on closures are uniformly applied by Pneumatic Rotary Capping machines which keep the containers moving smoothly at speeds up to 120 units per minute. The capped jars then move into the intakes of Pneumatic Duplex Labelers which simultaneously apply front and back labels, accurately registered and put on to stay.



8-head Pneumacap machine in operation at plant of Bunting Chemical Company.

Noxzema's new High Noon sun tan lotion is packaged in attractive plastic tubes. The tubes are filled and sealed at high speeds on a machine built by Pneumatic's Carbert Manufacturing Company Division. Another example of Noxzema's policy of keeping pace with the last word in packaging.



Front and back labels are applied simultaneously to Noxzema skin cream jars by duplex McDonald-type labeling units.

In its part of Noxzema's packaging processing, Pneumatic's modern equipment, built to fine precision standards with all the latest refinements in design, delivers the same "lower cost per container" operation which has attracted America's leading producers of bottled and packaged goods. Pneumatic could well help you to better, more economical bottling or packaging, too.

PNEUMATIC SCALE CORPORATION, LTD., 70 Newport Avenue, Quincy 71, Mass. Sales Offices: *New York; Chicago; Dallas; Rochester.* Agents: *Fred Todt Company at Los Angeles, San Francisco and Seattle. Rockwell Pneumatic Scale Ltd., Edgware Road, London, N.W. 2, England; O.R.M.A., Paris 8, France; Carbert Manufacturing Co., Division, Cambridge, Mass.; Delamere & Williams Co., Ltd., Toronto.*

PNEUMATIC

tion to its line of steam-jacketed kettles. This is the first time that a unit of this type has been made available in a pilot plant or laboratory size.

Scale System

Mercury Heat Sealing Equipment Co., 2601 North Howard St., Philadelphia 33, Pa. has developed a new hyperaccurate, high-speed scale system, called the Merco-Weigher.

Dual dribble and bulk feeds, running simultaneously in the last section, are operated by separate vibrators, permitting dribble feed to continue after bulk feed shuts off. Drop from scales to buckets is minimized to protect product. It also has an automatic control that stops the entire machine whenever any scale stops working.

Miniature Vacuum Recorder

Hastings-Raydist, Inc., Hampton, Va. has developed a new miniature vacuum recorder that is 3⅝ by 5⅝".

Chart paper and recorder scales are calibrated directly in absolute pressure units. The calibration is unaffected by exposure to, or changes in, atmospheric pressure.

Pressure-sensitive chart paper is marked by clamping bar action eliminating messy inks. Over 15 days operation is provided for on one roll of chart paper.

Gasketing Material

Armstrong Cork Company's Industrial Division has developed a new gasketing material that approaches a universal Aerosol valve stock.

The rubber compound, No.-773-A, eliminates for most applications, the need for having both a neoprene and a Buna N stock.

Drum Warmer

Dean Products, Inc., 1048 Dean St., Brooklyn 38, N. Y. has developed a new type of Panelcoil drum warmer. A 55-gal. drum is set horizontally in a cradle consisting of two semi-cylindrical sections of Panelcoil, which are permanently mounted on a steel structure. The top and bottom sections fit snugly against the smooth inside surface of the curved panels, leaving the middle section accessible for possible withdrawal of fluid contents. Hot water or steam at pressures to 125 psi (or refrigerant, if cooling is desired) is introduced into the single-embossed panels, circulating through the series of flow channels and out, transferring the heat to (or absorbing it from) the drum.

Automatic Product Filler

National Instrument Co., 2701 Rockwood Ave., Baltimore 15, Md. has developed a new volumetric-type product filler for aerosol lines that fills up to 40 16-ounce containers per minute. The Filamatic Model DRB-16 may be used for pressure or cold filling on new or existing aerosol lines.

All liquid contacting parts are fabricated of type 18-8 stainless steel and Teflon. A ¼ h.p. gearmotor and thyratron type electronic controller provide a 10 to 1 speed range.

Rotary Filler

Frazier & Son, 20 Industrial West, Allwood Clifton, N. J. has developed a new adaptation of their automatic Whiz-Packer. The Model CF Whiz-Packer can be constructed for limited speed operation with production of 60 or fewer units per minute, or for high speed requirements with a peak output of 300 units per minute. It handles containers ranging in size from ¾" dia. by 2" high, to 4" dia. by 7" high. The intake conveyor raises the container for contact with a filling spout. The product is supplied to the filler over a controller feeder tray and then delivered directly to the filling spouts. The container is then lowered from the filling spout and passes via the output conveyor onto the line for closure. The machine is powered by two ¼ h.p. motors. Folding is done as the plastic moves across a pair of heated die bars.

Automatic Pallet Loading Machine

Alvey Conveyor Manufacturing Co., 9301 Olive St. Road, St. Louis 24, Mo. has developed the Series 300 Pallet Loader that automatically arranges and places packages on a pallet in a pre-determined pattern and quantity. The machine will handle a conventional seven case pattern at the rate of approximately 39 cases per minute. It features the installation of all accessory components, and the elimination of possible package damage by not requiring each row of a layer to push the preceding row. The unit can be synchronized with other packaging machines or operated as an independent unit.

Label Printer

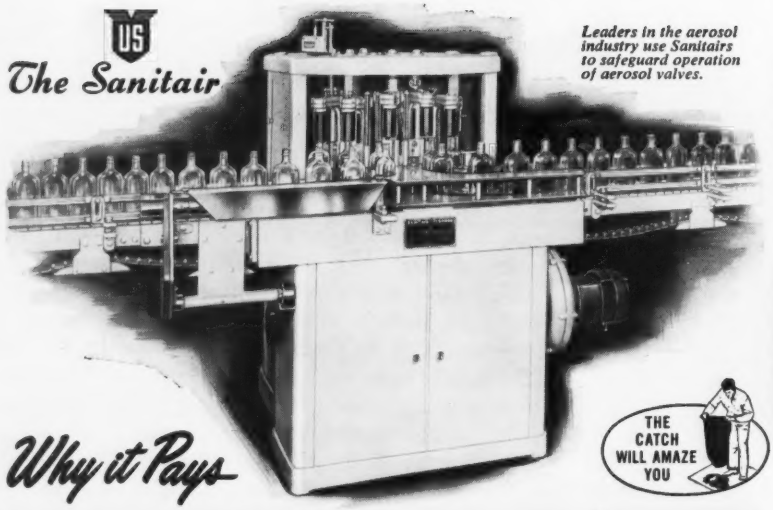
Sohn Manufacturing Co., Inc., Box 87, Plymouth, Wisc. has developed a machine that prints and die cuts in one operation on pressure-sensitive, gummed, heat seal or tag stock, as well as foil and fabric. The rubber printing plate is set inside a rotary die, giving exact registration. The machine is 9 x 9 x 9", and is constructed of aluminum and steel with rubber feet.

Flange Forming Machine

Tronomatic Machine Manufacturing Corp., 25 Bruckner Boulevard, New York 54, N. Y. has introduced a new continuous plastic double flange forming machine, capable of folding up to 3,000 blisters per hour. Known as Model C, it makes 90 or 180 degree flanges on any thermoplastic .005 thick and higher and folds blisters to accommodate cards from 1¼" in width up to a maximum of 14", with card thicknesses up to ⅛". It measures 100 x 30", is 44" high and weighs 750 lbs. All the accessory components such as motors, hydraulic pumps and control panels are within or on the main machine frame.

US

The Sanitair



Leaders in the aerosol industry use Sanitairs to safeguard operation of aerosol valves.

Why it Pays

TO REMOVE FOREIGN MATTER FROM NEW CONTAINERS

Packaging engineers demand it as indispensable to quality control. Merchandising managers demand clean containers for profitable consumer relations!

Air-Cleaning costs so little . . . the lack of it can cost so much. Once a Sanitair is synchronized into the production line, its operation is entirely automatic. Containers are completely inverted, *before, during* and *after* the air tubes enter, assuring positive cleaning. Has automatic operating safeguards. Speed is adjustable to line operation. Container changeover for all sizes including wide-mouth finishes. Exclusive, patented features. For complete details, write for the "Sanitair Bulletin."

U. S. BOTTLERS MACHINERY COMPANY

PACKAGING ENGINEERS

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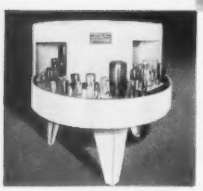
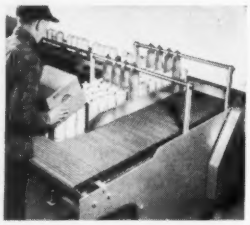
The E-Z Air Cleaner

for semi-automatic air cleaning of new containers of any size or type. Containers are manually inverted over air valves, two at a time, up to 40 per minute. Write for the "E-Z Bulletin."



For rinsing bottles or jars, ounces to gallons as illustrated. Rinses both inside and outside with water or steam. Write for the "Rotary Rinser Bulletin."

To Feed Containers Faster



THE U. S. CONTAINER FEEDER feeds containers to the packaging line faster, easier, at a steadier pace and a lot cheaper! Just dump 'em on, and let the feeder take charge. Pays for itself quickly and reduces costs permanently. Write for a "Container Feeder Bulletin."

Mettler

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FOR RAPID AND PRECISE WEIGHT CHECKING OF SMALL OBJECTS

Capacity: 10 grams, entirely on optical scale

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Magnetic damping

Also available with built-in set of weights to bring capacity to 160 grams. (Designation: Type H 23)

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Patent thoughts and trends

BY THOMAS CIFELLI, JR., PATENT ATTORNEY*

More on Utility in Drug Cases

From time to time we have considered the increasing demand made upon patent applicants in drug cases as regards requirements for stating the usefulness or utility of the compound or of the drug disclosed in a patent application. This subject has many facets. One is whether there is any disclosure at all of utility. In such cases the patent applicant fails to obtain his patent. Another important phase is whether the utility is actually proved. It is with this latter phase that the present article is concerned.

In spite of the fact that the authoritative Court of Customs and Patent Appeals has twice within the last four years handed down liberal decisions on this subject, the most recent decision, this one by the Patent Office Board of Appeals, takes a different slant. While the Board is on a lower level than the Court, as a practical matter the Board's rulings are quite important—at least until overruled.

In the first of the Court decisions referred to, the Court ruled that it was not necessary to show utility by way of tests on human beings in connection with a compound that was disclosed as an anti-spasmodic, where tests on animals showed the desired pharmacological effect. The Court reasoned that the patent applicant disclosures did not require that the compound be used on human beings. This is so, even though the Court pointed out that the actual disclosures described the compound as "useful in the form of their water-soluble non-toxic salts as anti-spasmodic agents" and also as "having mydriatic activity." The Court pointed out that Webster's New International Dictionary defined "anti-spasmodic" as "having a sedative effect on the nervous system; preventing or allaying spasms or convulsions." The same authority defines "mydriatic" as "causing dilation of the pupil." The Court felt that neither definition was limited in terms to either therapy or effects on human beings as distinguished from other animals.

In the second of the above-mentioned decisions of the Court, it ruled that animal experimental data were sufficient to show the practical utility of the compound there involved. These compounds were used in the X-ray examination of the gall bladder since they are opaque to X rays. The application in question disclosed the utility as follows:

"The new compounds are useful as X-ray contrast media, and are particularly valuable as cholecystographic agents . . . The compounds of my invention have been found to be more effective in producing shadows of the gall bladder than alpha-phenyl-beta-(4-hydroxy-3, 5-diiodophenyl) propionic acid which is currently the cholecystographic agent of choice . . . the compounds . . . when administered orally to cats in a dose of 100 mg. per kg. of body weight, gave excellent shadows of the gall bladder in X-ray pictures . . . No toxic manifestations in the cats were observed."

This case was previously discussed in this column, at which time it was noted that, even though the Court pointed out that the applicant's objective was to establish that the compound would be effective to diagnose human gall bladder diseases, nevertheless, the Court felt that animal experiments were sufficient to show the practical utility of these compounds.

We now come to the most recent decision in which the Board of Appeals of the Patent Office refused to follow either of the court cases referred to, ruling that animal experiments were insufficient to support the utility therein disclosed. In this last case it appears that the patent specification pointed out that the compounds (1) had use as herbicides, deweeding agents; (2) had use as inhibitors of the growth of yeasts—and thus was useful in isolation of bacteria from mixtures containing yeasts; and (3) contained the following paragraph:

"The compounds of the invention also possess unique properties in that they inhibit the biosynthesis, by living cells, of essential nucleic acids and nucleic acid precursors and also exert an inhibitory effect upon the growth of neoplasms. The inhibitory effect of L-6-diazo-5-oxonorleucine is greater than that of the corresponding DL and D-compounds; the DL-compound, in turn, possesses a greater inhibitory effect than the D-compound. The growth of implanted tumors in mice or rats is grossly inhibited by daily injections of L-6-diazo-5-oxonorleucine. The varieties of tumors which are so affected include Sarcoma 180 (liquid and solid forms), Sarcoma T 241, SarcomaMA 387, Mammary adenocarcinoma E 0771, Miyono adenocarcinoma, Mecca Lymphosarcoma, Ridgway osteogenic sarcoma, Wagner osteogenic sarcoma, RC mammary adenocarcinoma, Ehrlich carcinoma (liquid and solid forms), Carcinoma 1025, Krebs 2 carcinoma (fluid form) and Murphy rat lymphosarcoma. These u n u s u a l properties indicate that the products may be of possible value either alone or in combination with other neoplasm-inhibiting agents such as 6-mercaptopurine in the treatment of neoplastic diseases (carcinomas, sarcomas, leukemias, etc.). The products may be administered by either the oral or parenteral routes."

It appears that the Examiner would have allowed the claims if the statements of utility had been limited to (1) and (2) above. He felt, however, that in the presence of the statement of the third utility, which "may be interpreted as im-

*Richards and Cifelli, Newark 2, New Jersey

plying utility in the treatment of cancer in humans," the claims could not be allowed, unless the applicants furnished conclusive proof of such implied utility, that is, clinical evidence on human beings.

The patent applicants contended that the issue was simply whether product claims directed to a chemical compound admittedly patentable over the prior art and admittedly based on an adequate proved utility can be validly refused because the specification contained, *in addition* to a proper statement of utility, some other statement of utility which has not been proved beyond any possibility of doubt.

In determining the issues in this case, the Board relied on the following rule taken from an earlier case:

"In order to sustain a patent it is only necessary that a single utility be disclosed. In this case we see no objection to retaining references to the other proposed uses unless they are incredible or misleading."

Also, since this case dealt with medical subject matter, the Board felt that, in the words of a court in another case:

"Great care and scrutiny should be particularly taken in connection with applications for medical patents. While the granting of a patent does not legally constitute a certificate that the medicine to which it relates is a good medicine and will cure the disease or successfully make the test which it was intended to do, nevertheless, the granting of such a patent gives a kind of official imprimatur to the medicine in question on which as a moral matter some members of the public are likely to rely. In view of these circumstances, it is right and proper that the Patent Office should be very careful and perhaps even reluctant to grant a patent on a new medical formula until it has been thoroughly tested and successfully tried by more than one physician. It seems to the Court that therefore the Patent Office, as a matter of public policy, followed a proper course in this matter."

The key question in the view of the Board is whether the disclosure given in the above-quoted paragraph was in fact misleading. The Board answered this question in the affirmative. It felt that members of the public reading the quoted paragraph would conclude that the claimed compounds possess utility in the treatment of cancer in humans. In the words of the Board:

"The first two sentences of the paragraph are general as to the 'unique properties' of the compounds in inhibiting the biosynthesis, by living cells, of essential nucleic acids and their precursors and the growth of neoplasms. The next two sentences relate to this inhibitory effect with respect to implanted tumors in mice. The paragraph concludes by stating that these 'unusual properties indicate that the products may be of possible value' in the treatment of cancerous diseases and that the 'products may be administered by either the oral or parenteral routes.' While human treatment is not specifically recited, neither is it excluded and we think a fair interpretation leads one to conclude that it is intended, particularly since no commercially v a l u a b l e animals which could be considered objects of this utility within the meaning of 35 U.S.C. 101 and 112 are mentioned. Mice and rats are not in such category, since, in our observation, these have been used merely as experimental or test animals in preliminary steps leading up to an evaluation with respect to humans or commercially valuable animals and not as having in themselves sufficient economic value to warrant treatment."

In refusing to follow either of the Court's decisions, the Board pointed out that neither of them contemplated any *treatment* of disease but one dealt with an anti-spasmodic and the other with an X-ray contrast agent; whereas in the case before it, a very serious disease, cancer, was involved.

Whether the recent Board decision will stand up on appeal to the Court of Customs and Patent Appeals, if such an appeal is taken, of course, is open to question. However, the lesson to be learned from this Board case is that sometimes it is good to know when to stop. Without question, if the quoted paragraph had been omitted from the application there is no doubt that the patent would have been obtained with the claims in question. If any statement as regards utility indicates an intention to use the products on human beings, one should be prepared to show by suitable tests on human beings that the products are useful. Animal tests are not enough.

On Being a "First" Inventor

It is believed that we are all guilty of oversimplification at times. In the field of patents, for example, one may be pardoned if he states that, in order to obtain a patent, progress over the prior art should be shown. However, as was recently pointed out, one of the judges of the Court of Customs and Patent Appeals called this an "unsound notion." All that is required, according to this view, is to show an unobvious result.

Even such a "safe" statement as, "One has to be a first inventor of a thing in order to obtain a U. S. patent," is not always correct. For example, if a prior worker in the field made an invention, used it privately and secretly and then abandoned it, a subsequent worker who is ignorant of his predecessor's accomplishments but who is an original inventor, in the sense that he made the invention himself, may secure a valid patent. Another example of an exception, is that of a lost art. There are many arts that have become extinct and forgotten for ages. A person who rediscovers one of them may be entitled to a patent if the subject matter were otherwise patentable, in spite of the fact that obviously he would not be the first inventor. One court has suggested an interesting question which might arise if an artist who paints and constructs stained glass windows were to rediscover and devise a rose-colored pigment, now unknown, but which was used with buildings of medieval cathedrals. Would the pigment be patentable?

Another exception to the rule that one must be the first inventor to obtain a patent is the case where the invention is first made in a foreign country and is neither patented nor described in a printed publication. A subsequent original inventor in this country may obtain a valid patent. Again, it should be pointed out that the subsequent inventor must be an *original* inventor. Thus, if a person on a trip to Europe learns of a certain product and, on his return to the U. S. A., attempts to patent it, he would not be able to obtain a valid patent, because the invention would not be original with him.

(*Continued on page 260*)

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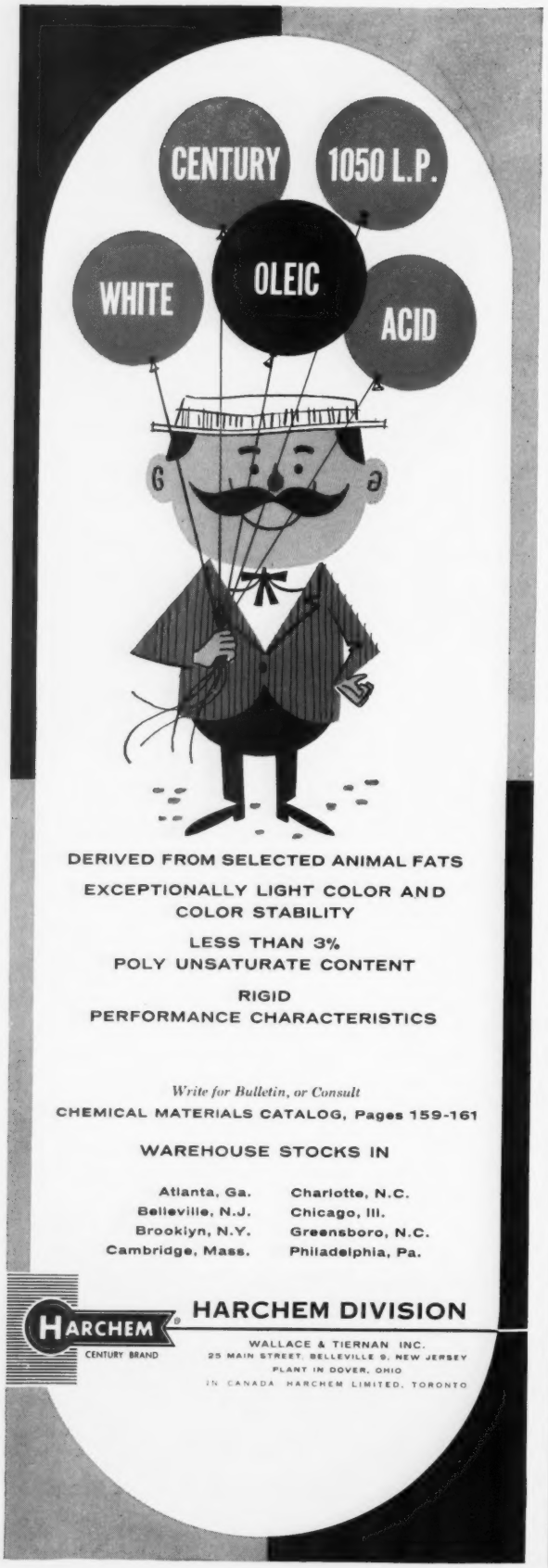

(*Continued from page 161*)

earnings increased "substantially" during 1959. In Europe, distribution was expanded in France, Italy, and Switzerland, and new manufacturing plants were established in South Africa and Argentina. Revlon now has local manufacturing operations in eight countries. The company, which earned $10,800,000 in 1959, reported that the combined net earnings of its foreign subsidiaries and branches in 1959 totaled $1,800,000.

Avon. Locked in a fight with Revlon for volume leadership in the cosmetic industry, Avon also is a recent discoverer of foreign markets. From all reports, though, Avon has been able to duplicate overseas its amazing success in the U. S .(sales up 155 per cent in the past five years). The company now does 6 per cent of its $140,000,000 volume outside the U. S. and Canada. Operations have been mounted in Puerto Rico, Cuba, Venezuela, Mexico, Germany, Brazil, and Britain. Seasoned veterans of the international wars will tell you that if anyone had asked them in advance whether a house-to-house operation would work overseas, they would have said: "You're crazy. It will never go. Not in a million years."

Avon has proved them dead wrong. In Cuba, before Castro nationalized everything in sight, it took Avon only two years to reach a volume that had taken other U. S. companies decades to build up. The Avon blitz is a sudden one. Since its sales are made house-to-house, its penetration does not show up in any store audits. As one international marketing executive told me, "You just wake up one morning and find your sales have evaporated."

Beauty Counselors. This is another house-to-house operation that has moved abroad. The company did $10,000,000 volume in 1960 for the first time, and now has operations in England, Venezuela, and Mexico. It had also been marketing in Cuba.

Shulton. This company, which features a moderate-priced line, increased its total sales from $24,900,000 in 1955 to $43,700,000 in 1959—and international expansion made a major contribution. In 1959 alone, its foreign sales were up 40 per cent and now account for more than 15 per cent of total volume. Shulton entered the French market in 1959, its British company has invaded Australia, and it has recently put up new facilities in Argentina, Mexico, Venezuela, and the Netherlands.

Helene Curtis. Active in overseas markets for some 20 years, this company operates primarily through licensing agreements with foreign companies. For its fiscal year ended Feb. 29, 1960, the company reported income from foreign commissions and licensing of $542,640, which represented about 10 per cent of profits before taxes. This exceeded the company's *total* net income for the year 1957. John R. Torrens, vice president of Helene Curtis International reports that "the company is at the present time engaged in activities which will lead to strengthening

and developing the overseas operations." Helene Curtis products are now distributed in some 60 countries.

Bristol-Myers. This drug and toiletries company reported total foreign sales of $25,138,000 for 1959. Consolidated net income from foreign operations totaled $1,944,000. Foreign sales of proprietary products were up 20 per cent in 1959, mainly as a result of increased volume of deodorants, marketed abroad under the brand name, Mum Rollette. The company recently bought a German outfit, Khasana, and is building a new plant in Frankfurt. It is doubling the size of its British plant. Contributing to the overseas surge is its newly acquired Clairol, which has subsidiary operations in Canada, Britain, Venezuela, Italy, and France.

In addition to the companies listed above, there are diversified manufacturers with cosmetic business buried in consolidated sales statements—several of them potent marketers abroad. The Gillette Company, for example, has its Toni division, and Gillette is a company that now derives 50 per cent of its net income from foreign operations. And then there is Colgate-Palmolive, with Lustre Creme and Halo. Colgate has imposing foreign sales of $300,000,000 and foreign earnings now represent 64 per cent of total net income!

The next five to ten years are expected to be interesting ones in the international cosmetics business. Close observers of the scene predict heightened competition. They also see many more mergers coming, as the international giants scramble for a share of the increased volume expected in countries where the standard of living is rising sharply. Cosmetics volume is closely associated with standard of living (in Britain, for example, they are only now beginning to pay attention to the "youth market"), and from this standpoint, the future looks rosy. But there are many eyes peering into this crystal ball. Don't wear rose-colored glasses—and keep your guard up.

TOPICAL THERAPY

(Continued from page 163)

I am not altogether certain that we yet know enough regarding potential hazards of long-term and widespread use of topical antibiotics to be able, with safety, to incorporate them into acne proprietaries. The responsibility for demonstrating safety with prolonged topical application rests with those who want to promote their use in a proprietary.

We face similar problems in the possible incorporation of topical corticosteroids into such products. There is little doubt about the usefulness of small amounts of hydrocortisone and some of its more potent derivatives in treating the inflammatory phases of acne lesions. Yet our critical information is inadequate for the safe incorporation of cortico-

(Continued on page 232)

KNAPP FINE CHEMICALS PRODUCTS INC.
LODI, NEW JERSEY

- **EMULSIFIERS**
- **DETERGENTS**
- **ABSORPTION BASES**
- **FRAGRANCES**

- **SCIENTIFICALLY DEVELOPED AND MANUFACTURED— SPECIFICALLY FOR APPLICATION IN COSMETIC FORMULATIONS**

KNAPP FINE CHEMICALS PRODUCTS INC.
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Here are fast facts about **PANTHENOL:**

Just what is **PANTHENOL***?*

PANTHENOL is the alcohol of pantothenic acid, an important member of the vitamin B-complex.

What will **PANTHENOL** *do in my formulas?*

PANTHENOL helps to soothe and heal chapped, rough skin; promotes normal growth of skin and mucous membranes; helps groom and keep hair healthy, lustrous, and attractive.

Is **PANTHENOL** *safe?*

Yes. Dermatologists and other members of the medical profession have prescribed PANTHENOL for years. They have administered PANTHENOL topically, orally, and by injection. Numerous reports published in medical journals confirm the safety and usefulness of PANTHENOL.

What other advantages?

All these: PANTHENOL is stainless, water-washable, harmless to lips, skin and hair. It's stable, and can be combined with other vitamins, such as A, B_6, D and E.

Who makes **PANTHENOL***?*

PANTHENOL is made by Hoffmann-La Roche Inc., a pioneer in the synthesis, development and large-scale production of many of the most important vitamins.

Tell me a few uses for **PANTHENOL.**

You'll find PANTHENOL particularly valuable in cosmetic and toilet goods formulas, such as:

Lipsticks	Hand Lotions	Hair Tonics
Face Creams	After-shave Lotions	Deodorants
Body Creams	Hair Sprays	Anti-Perspirants

Can I use **PANTHENOL** *with my present equipment?*

You can incorporate PANTHENOL into your formula with your standard equipment.

Where do I get complete information about **PANTHENOL***?*

From Roche! Get free informative, helpful literature by contacting your local Roche representative. Or send your inquiries directly to the Roche Technical Service Department. Send today.

Available on request—"Panthenol in Cosmetics", by S. H. Rubin, L. Magid, and J. Scheiner, reprinted from Proceedings of the Scientific Section of The Toilet Goods Association, Number 32, December, 1959.

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Compounder's Corner

Antioxidants

Oils and fats are particularly liable to suffer spontaneous deterioration in the presence of air—the reactions taking place, generally called "oxidative rancidity" or autoxidation, cause changes in odor and taste. The alteration in these properties is at first subtle and unnoticeable, but gradually becomes more pronounced until a distinct and characteristic "off" odor and flavor is evident. The autoxidation process is not confined to fats and oils themselves, but can also occur in a wide range of products containing them, and this rancidity seriously affects their market value.

Many techniques, including vacuum packing, refrigeration, and inert gas packing, have been tried, to combat oxidative degradation; but one of the cheapest and most effective methods is the use of chemical antioxidants. By incorporating a very small proportion of a suitable antioxidant in a fresh fat or oil, the autoxidation process is effectively inhibited, and normally highly perishable commodities can be stabilized for periods well in excess of their ordinary useful life. Although they provide a means of extending the useful life and retaining the original properties of flavor and odor of fresh fats and oils, antioxidants will not restore freshness to, or improve the keeping qualities of, partially oxidized fats.

The chief antioxidants used today are the gallic acid esters, from methyl to stearyl, of which the most popular is propylgallate (P.G.); butylated hydroxyanisole (B. H. A.) first officially used in the U.S. in 1948; and butylated hydroxytoluene (B.H.T.) used for long in petroleum products, but in refined grades now used widely in animal feeding stuffs and other food products. Smaller quantities of the higher gallates, nordihydroguaiaretic acid (NDGA), and the tocopherols (vitamin E), are also used.

Any antioxidant should be effective at low concentrations, easy to incorporate, remain active after normal cooking or processing, be readily available, and of low cost. In addition it should not impart any odor, color or flavor to the products treated, and above all it and its reaction products must be absolutely harmless to health at the concentration used.

Combinations of two or more antioxidants are often synergistic, that is, the components reinforce each other and the antioxidant activity of the blend is greater than the sum of the activities which each individual component would exert at equivalent concentrations alone. Such synergism is shown by combinations of B.H.T. and B.H.A., and B.H.A. and propyl gallate, but not by B.H.T. and P.G.

Certain acidic substances, phosphoric, and especially citric acid, and its esters (lecithin and oleyl) also exhibit a kind of synergism when used with true antioxidants such as B.H.A., B.H.T., or P.G, Having little or no antioxidant activity of their own, these acid synergists seem to function by forming complexes with traces of metals such as copper and iron, which are oxidation catalysts, and by suppressing the pro-oxidation effects of these, increase the efficacy of the primary antioxidant. The elimination of trace metals from a fat, or the complete suppression of their pro-oxidant activity can indeed be quite as important a factor in the stability of the fat as the addition of an antioxidant. Even in the absence of metals, addition of these acids ensures that the limited amount of antioxidant permitted, gives its fullest benefit.

Most cosmetic preparations contain components which are prone to oxidation on exposure to air, and the use of an antioxidant will provide a valuable safeguard against this kind of deterioration.

Oxidative deterioration in cosmetics during long storage may show in a number of ways: as typical "off" odors and flavors, discoloration, increase in or loss of color, or loss of odor. Some perfumery ingredients such as heliotropin, eugenol, coumarin, vanillin, and methyl anthranilate are easily oxidized and themselves function as antioxidants. Although superficially beneficial, oxidation of these compounds may be accompanied by such esthetically undesirable side effects as loss or alteration of fragrance, or discoloration. The autoxidation process decomposes not only animal and vegetable fats, oils and fatty acids, but other ingredients such as sterols (cholesterol); lanolin and its acids (the acids are more oxygen sensitive than lanolin alcohols); various essential oils; petroleum jelly, waxes and refined mineral oils containing unsaturated hydrocarbon compounds, also undergo changes in odor and physical properties.

The requirements of cosmetic antioxidants are generally similar to those for food use, but in addition they must not give rise to any local toxic or dermatological effects. Besides being well tolerated by the skin they should have little odor or color; be unaffected by light, heat, moisture and free acids; and they must preserve the distinctive qualities of artistry and elegance characteristic of cosmetics; and effectively prolong the shelf life of the product.

The smallest effective quantity should be used, to avoid risk of toxic absorption or local skin reactions. B.H.A. and B.H.T. are excellent for cosmetics, alone or admixed. Addition of a gallic ester further improves the protective effect, especially in creams containing vegetable oils, vitamin A, or monoglycerides. Citric and phosphoric acids, polyphosphates, and lecithin may be added to these antioxidants as synergists to enhance their effect.

Castor oil widely used in lipsticks for its solvent and thixotropic effect is ordinarily fairly stable to oxidation, but in the presence of bromoacid and lake dyestuffs may quickly go rancid. Lipsticks often have a long storage period and time of use, and so the incorporation of an antioxidant or synergistic mixture is most desirable.

The wool alcohols and lanolin are also extensively employed as emulsifying agents in cosmetic creams, ointments, and lotions. The chief constituents of lanoline are wool fat sterols such as cholesterol, in the form of higher fatty acid esters. Immediately after manufacture the product is almost white and has a peroxide value of zero. After 6-12 months the color becomes yellowish, P.V. rises to 50-150, and a characteristic "off" odor is noticeable. Trace metals in the fat accelerate this oxidation, which also causes a rise in acid value of the oil phase, and a reduction of sterol content. Under these conditions creams containing such oxidized lanolin are likely to "crack" and separate. Addition of a phenolic antioxidant such as B.H.A. immediately after refining, to the still molten fat, will retard autoxidation. The hydroperoxides in a batch of lanolin at an advanced stage of oxidation may be broken down by heating for a few hours under vacuum at 150 deg.C, reducing the peroxide value to 5 or less—the material can then be stabilized like fresh lanolin, by the addition of antioxidants.

Oil/water emulsions are common in pharmaceutical and cosmetic use, and are present in such foods as margarine, butter, mayonnaise and dairy cream. Oxidative deterioration in these is often very rapid because of the large surface area of the dispersed fat phase. Little is yet known of the ability of antioxidants to stabilize these complex oil/water systems, but it seems that the presence of water decreases the activity of water-soluble antioxidants, but actually increases that of the fat soluble antioxidants, but actually increases that of the fat soluble ones. Thus antioxidants with a high oil and fat solubility and a high oil/water partition coefficient are the most effective in emulsions. Increase of *p*H of the aqueous phase from 5.1 to 9.2 decreases the activity of even fat-soluble antioxidants, and at higher (alkaline) *p*H, the stabilizing effect is absent, and no advantage accrues from their use. High fat-soluble antioxidants give best results in emulsions with neutral or acid aqueous phases. The addition of water-soluble synergists such as citric acid does not provide any extra stability in such neutral/acid emulsions, but fat soluble esters like monostearyl, or monoisopropyl citrate, or ascorbyl palmitate, are effective here.

Essential oils for cosmetics, perfumery and flavoring show marked differences in their tendency to oxidize during storage. Fennel, lavender, orange and lemon oils oxidize very readily, rosemary and bergamot are rather more stable, while clove and cinnamon oils are quite stable to oxidation. The most important qualities of an essential oil, its characteristic taste and odor, are unfortunately those that suffer most when the oil is affected by oxidative rancidity. This is mainly due to decomposition of the terpene, sesquiterpene and polyterpene content of the oil. Storage at reduced temperature (optimum 4 deg.C) can be used to prolong shelf life, but when this is neither possible nor convenient, the addition of an antioxidant such as nordihydro-guaiaretic acid, propyl gallate or B.H.A. will usually provide satisfactory stability.

Many essential oils contain traces of heavy metals such as iron and copper (oil of fennel can contain up to 0.001 per cent Fe) which reduce the efficacy of added antioxidants, and also cause the production of red or yellow discoloration. Citric acid will deactivate such metal traces and also synergize the primary antioxidant. An optimum addition of antioxidant to essential oils is 1 part in 1,000, but less (0.01 per cent B.H.A. in fennel) often suffices. Citric acid up to 0.05 per cent is commonly used with B.H.A., or B.H.A. and P.G.—*Chem. Prod.* 23: 541, 1960.

Weight Reduction Diets

Starting with the 900-calorie Metrecal powder, an almost endless procession of weight reduction dietary products have been marketed. These are powders to be made up into liquid preparations by the addition of water to make one quart, or premixed liquids. One day's feeding should contain 900 calories or so, instead of the normal intake of 2500 and more (often much more) calories, and from 50 to 70 grams of high-quality protein, preferably along with minimum daily requirements of vitamins and minerals. The secret behind these preparations is partly psychological, since with minimum effort the dieter knows that she is taking in the prescribed amount of food and cannot cover up cheating, and partly physiological in that the liquid diet keeps the stomach at least partly distended and thus reduces hunger pangs.

Two major improvements in these products seem evident. The first has already been covered in liquid preparations put out by dairy companies—reduce cost by providing a lesser amount of dietary powder to be mixed into one quart of whole milk, calculating the powder to make up vitamins, minerals, and proteins deficient in the milk. Perhaps more important is the need to counteract the deficiency of bulk in this liquid diet, which often leads to some degree of constipation. This ought to be easily taken care of by adding the proper proportion of carboxymethylcellulose or other bulk producing gum which, in addition, might add "body" to the liquid diet, and thus somewhat increase its acceptance. J.K.

John Robert Powers offers two new products, Biocenta Treatment Cream and Bio Tonic Masque containing placenta extract.

Charles of the Ritz is introducing three salon hair care products, shampoo, hair conditioner, and hair spray. The concentrated shampoo contains yuccarone, extracted from yucca plant root, is neutral in reaction and is available in a formula for dry or tinted hair and one for oily hair in 5 ounce plastic bottles. The Hair Sheen is an emulsion hair conditioner and dressing supplied in one ounce plastic tubes, while the aerosol hair spray comes in a 5 ounce can.

Northam Warren include cholesterol and "white iodine' in Nail Flex for nail care. It is packaged in a purse-size polyethylene tube.

LeMur is distributing Blem-Aid, a medicated cream containing polythionates, is intended for the relief of acne pimples and related skin blemishes. The cream is non-greasy, quick-drying, odorless and flesh-tinted and is supplied in a plastic squeeze bottle.

Roux Fanci-Tone is packaged in 2 ounce tubes for blonde toning; one ounce is to be mixed with 3 ounces of peroxide before use. The product is available in forms to provide six light shades. The Roux Hairdressing is packaged in a 2 ounce tube.

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TRADE LITERATURE

Polymer-Coated Films. American Viscose Corp., Film Div., Market Development Dept., 1617 Pennsylvania Blvd., Philadelphia 3, Pa.—4-pg. brochure outlines characteristics and uses of improved polymer-coated films.

Pneumatic Conveyors. Young Machinery Co., Muncy, Pa.—3-pg. illus. bulletin (P-259-A) describes negative and positive pressure systems, closed circuit system, and special applications.

Citric Acid. Miles Chemical Co., Elkhart, Ind.—30-pg. illus. brochure lists grades of citric acid available, its physical and chemical properties, and their applications.

NYQ Product List. NYQ Chemical Div., S. B. Penick & Co., 100 Church St., New York 8, N. Y.—68-pg. illus. catalog lists more than 300 items, with sections on antibiotics, chemicals, narcotics, vitamins, and information on mesh specifications, forms and grades available, packing.

Plastic Packages. Monsanto Chemical Co., Plastics Div., Springfield 2, Mass.—12-pg. illus. booklet discusses merchandising, product preservation, and cost factors of plastic packaging.

Siphon Filler. U. S. Bottlers Machinery Co., 4015 North Rockwell St., Chicago 18, Ill.—4-pg. illus. bulletin describes siphon principle, filling tubes, starter, and the Siphon Filler.

Screw Conveyor Equipment. Thomas Conveyor Co., Dept. 106, Box 11127, Fort Worth, Texas—150-pg. guide shows screw conveyor installations, charts, and additional products.

Plastic Packages. Extruded Plastics, Inc., New Canaan Ave., Norwalk, Conn.—illus. folder and price list describes Tulox packaging materials and methods.

Labelers. New Jersey Machine Corp., 16th St. & Willow Ave., Hoboken, N. J.—Brochure describes labelers for round glass and oddly shaped containers.

Pearl Pigments. Rona Pearl Corp., div. of Rona Laboratories, Inc., East 21st & East 22nd Sts., Bayonne, N. J.—12-pg. brochure covers properties, typical uses, and general application procedure, with sections on coating, casting, compounding and cosmetics.

Tablets and Capsules. Nysco Laboratories, Inc., 34-24 Vernon Blvd., Long Island City 6, N. Y.—44-pg. catalog lists Nysco's services, tablets, and capsules.

Onyx Products. Onyx Chemical Corp., 190 Warren St., Jersey City 2, N. J.—23-pg. catalog lists more than 100 surfactants and specialty products with their chemical and physical descriptions.

Tenite Packaging. Eastman Chemical Products, Inc., Kingsport, Tenn.—20-pg. illus. booklet describes packaging materials based on tenite plastics.

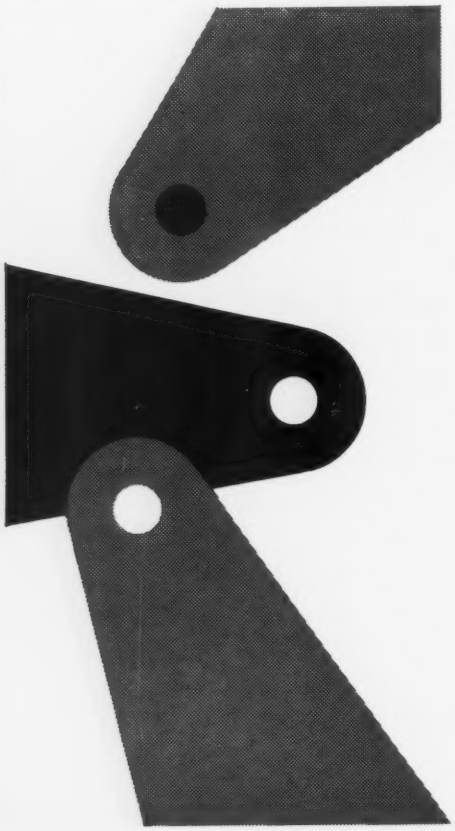
The Folding Carton. The Folding Paper Box Assoc. of America, 222 West Adams St., Chicago 6, Ill.—Illus. booklet features an extensive glossary of terms used in the manufacture of folding cartons and includes diagrams of the most popular styles, descriptions of the manufacture, and use of cartons.

"Codeine Today." Merck Chemical Div., Merck & Co., Inc., Rahway, N. J.—14-pg. booklet is an up-to-date review of the clinical significance of codeine and tells of its use in a wide variety of conditions for relief of pain or cough.

Screw Feeding Equipment. Vibra Screw Feeders, Inc., 156 Huron Ave., Clifton, N. J.—8-pg. folder describes the test performance of screw feeding equipment for 456 different dry materials from abrasives to zinc stearate.

Revolver Feeders. Fuller Co., Catasauqua, Pa.—2-pg. illus. bulletin (F-9) describes revolver feeders designed for feeding dry, pulverized, and granular materials into high-pressure pneumatic conveying systems with small diameter lines.

Electronik Recorders, Indicators. Minneapolis-Honeywell Regulator Co., Ind. Div., Wayne and Windrim Ave., Philadelphia 44, Pa.—48-pg. illus. catalog (#C 15-1a) describes strip chart recorders, circular chart recorders, precision indicators, and measuring elements.



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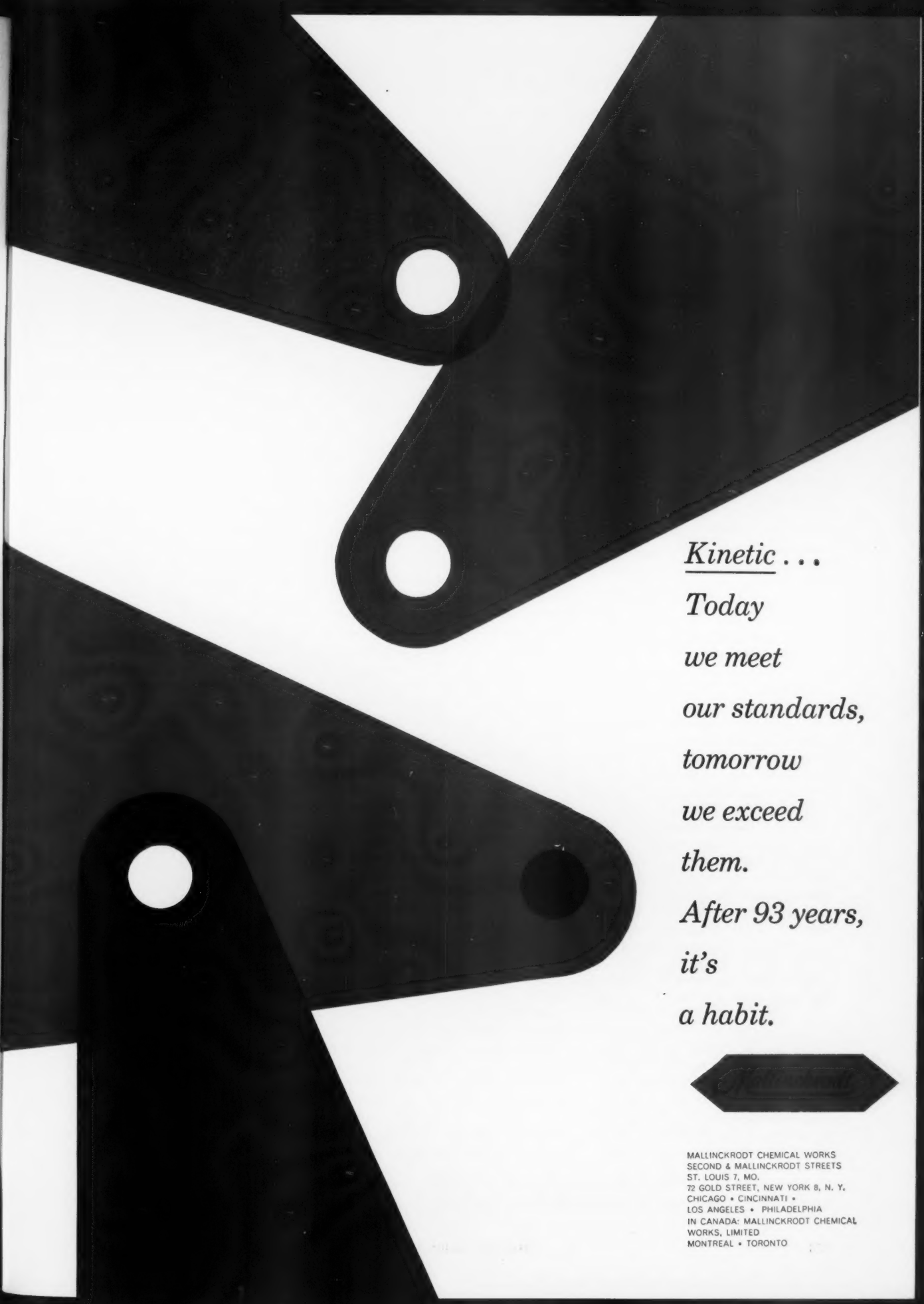

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Flavoring Pharmaceuticals

When deciding upon a flavor for a medicine there are a number of factors to be considered according to G. R. A. Short (*Manuf. Chem.* 1961, p. 15). Is it desired to just mask the unpleasant ingredients or to impart an overriding taste and odor? Is the medicine to be taken continuously over a long period, or will a few doses only be necessary? The flavor must be compatible chemically and it must be miscible with the vehicle; for example, an acid flavor such as a natural fruit syrup cannot be used with alkaline medicaments, and if a clear product is required in an aqueous medium, then a soluble flavor must be employed.

In a paper read at the Harrogate Pharmaceutical Conference in 1951, Eastland enumerated four methods of approach to the flavoring or masking of distasteful drugs: (1) To use a pleasantly flavored substance which has something in common with the drug; such as orange with gentian or quinine. (2) To use substances such as menthol or oil of peppermint to produce a mild local anesthesia. (3) To use colloidal solutions such as mucilage of acacia as a vehicle. The mechanism here is unknown, but it is an effective method in some cases. (4) To use moderate concentrations of sodium chloride in which the bitterness of some drugs is lessened. He states further that oil-soluble drugs can be dealt with by producing emulsions of the oil-in-water type, but the effect of emulsification is much less useful for water-soluble substances which will remain in the disperse phase.

The effect of effervescence, *i.e.* the production of carbon dioxide when the powdered or granular medicine is added to water, is well known as an effective method of taking certain unpalatable medicaments such as salines. Such products may be sweetened or unsweetened and may often be improved by the addition of flavors, particularly of the citrus type.

Flavoring pharmaceuticals is perhaps one of the most difficult problems confronting the flavor chemist, since members of his tasting panel are sometimes averse to testing drugs and moreover the taste buds are often readily immunized by the undesirable character of the medicine. In view of the fact that different people respond differently to the same taste stimuli, and that individual tasters are influenced by factors such as the time of day, environment, temperature, age, stress and strain and physical health, it is wise to employ an expert panel.

Most of the published work on the flavoring of pharmaceuticals has appeared in American literature, but since British tastes differ somewhat, it is useful to quote some specific examples.

Cod-liver oil emulsion was formerly flavored with almond, but useful variants of this are hazelnut, walnut, creamy caramel and butterscotch. Similarly, malt extract with cod-liver oil by virtue of its viscosity, color and basic flavor suggests the use of caramel and toffee flavors, vanilla and butterscotch. Blends of citrus oils with or without vanilla or almond are also useful. Cod-liver oil itself is difficult, but citrus oils such as orange or tangerine give reasonable results. Mineral oil emulsions having a bland character are improved by the addition of creamy flavors such as vanilla, marshmallow or cream soda, coupled with syrup or saccharin. Liver extract is a troublesome product and for this savory flavors such as celery, sage and mono-sodium glutamate are perhaps the best, but citrus and caramel flavors have been found useful. For alkaline digestive mixtures cream flavor, vanilla, aniseed, fennel and of course peppermint are satisfactory. Owing to the powerful adsorption of flavors on to the ingredients, indigestion powders are best aromatized with powder flavors. These powder flavors must be of the "sealed in type" which liberate their flavor only on moistening with water.

Linctuses having an acid reaction lend themselves to flavoring with fruit syrups such as cherry, raspberry, strawberry or black-currant. For best results fruit juice syrups should be used, these may be prepared from fresh juices, in season, or from diluted concentrates. As pointed out by Etchells these concentrates tend to darken in color on storage although the flavor is retained; it becomes necessary, therefore, to add color to the syrups produced from them. Should the cost of these syrups be considered prohibitive, then one must use essences together with the appropriate color in a base of acidulated syrup. Linctuses having a neutral reaction can be flavored with essential oils such as aniseed, fennel or cloves either singly or blended; for less stereotyped flavors passion fruit, black-currant, apricot and wine types can be employed.

Sulfa drugs are difficult, but saccharin together with a fruit flavor such as strawberry, raspberry, apricot or passion fruit is reasonably effective. Antibiotics in liquid form can be flavored with fruit flavors, particularly lemon, lime, orange and perhaps ginger, but for tablets and lozenges it is best to use powder flavors. An interesting point with regard to tablets which emit an objectionable odor when bottled is that this can be partially masked by treating the cotton-wool plug with a solution of vanillin and drying before insertion.

Invalid foods having a milk powder base can be improved by the use of caramel, butterscotch, vanilla, peach, apricot or black-currant powder flavors. For protein hydrolyzates pineapple, banana, caramel, honey, butterscotch and savory flavors are to be recommended. For amino-acids, spice flavors such as ginger or cinnamon are best. Powdered yeast preparations blend well with savory flavors and in some cases plum and vanilla can be used. Mixtures con-

taining the vitamin B complex can be improved with nut flavors such as hazelnut or walnut. Vitabin B_{12} is a rather special case for which flavors free from aldehydes are required.

The only satisfactory flavor for paraldehyde draught is peppermint. Preparations containing chlorides and other saline drugs can be improved with cream soda, maple or chocolate flavor. For barium meals butter and caramel flavors have been found to be useful.

Guaiacol and creosote are particularly difficult to mask, so for these powerful flavors such as peach or apricot are indicated. Guaiaphenesin blends quite well with syrups flavored with strawberry, blackberry, cherry, raspberry and caramel. A mixture containing senna extract was improved with a fig essence.

In conclusion the author stresses the importance, when formulating a new product, of conducting a storage test at room temperature and at an elevated temperature. This will demonstrate whether the flavor has changed and whether color fading has taken place. Don't over-flavor, over-color or over-sweeten. If it is decided to hand over a flavor problem to experts, give an indication of the constituents of the medicine if possible, and above all, state the proposed dose.

Oil Synthesis in Mint

Essential oils have been commonly thought to be end products of a long series of reactions. They would, therefore, be produced more slowly than other photosynthetic products. The formation also would be expected to be slow if the oils were simply by-products of normal plant photosynthesis. Comparative analyses of oils harvested at the start and the end of the growing season regularly show large differences between oils from young, actively growing plants and from mature plants. This difference also has been observed between young and mature leaves on the same plant. This might suggest a slow conversion of constituents throughout the growing season. Laboratory results by R. H. Reitsema, F. J. Cramer, N. J. Scully, and W. Chorney (*J. Pharm. Sci.* 50: 18, 1961) using labeling techniques lead to completely different conclusions. Initial exposures of three hours proved to be very long for oil synthesis. These oils from three-hour labeling experiments appeared to be uniformly labeled. They were not significantly different from oil labeled for seven days. A sixteen-hour exposure to low activity gave an auto-radiograph in five days which showed the presence of radioactive peppermint constituents, i.e., menthol, pulegone, menthone, and hydrocarbons.

The rate of oil formation was determined by reducing the length of exposure of the plant to the $C^{14}O_2$ atmosphere. Photosynthetic periods of three, seven, and fifteen minutes were used in one series of experiments. Only a small portion of the radioactivity is found in the oil, particularly in these short-term experiments, and it was necessary to run a greater concentration of radiocarbon and to run autoradiographs for several weeks. A sequence of formation of components of the oil is evident. The labeling and identification techniques used are adequate to show the formation of peppermint oil within fifteen minutes. This is a maximum amount of time for the formation of peppermint constituents from carbon dioxide.

The experiments were not sufficiently definitive to clarify the sequence of formation of peppermint oil constituents. Piperitone is present in the seven-minute oil and is dominant in the fifteen-minute oil. Its existence as an early constituent of peppermint has been anticipated by other work. Judged by the relative intensity of the radioactivity it can be suggested that menthol follows the appearance of pulegone, menthone, and hydrocarbons. The detection methods is not quantitative and the presence of a labeled component may indicate concentration rather than chronology.

A study was made to determine whether mint plants continue to produce oil after cessation of photosynthesis. Results indicate that oil formation can continue without photosynthesis, provided that the necessary precursors are present, for at least forty hours.

The relative rates of oil formation in the light and dark were not conclusively shown by the experiments. Experiment 2 indicated that the plant put in the dark for three hours after exposure to labeled atmosphere produced an oil with three times as much radioactivity as did the plant put in the light. Experiment 8, however, indicated no real difference in a similar experiment.

The amount of oil lost from a mint plant has practical significance. The intensity of the odor in the neighborhood of a mint field would suggest that this is an appreciable quantity. Although the simulation of a natural growth situation was not attempted, an idea of the quantity of oil lost was obtained by radiocarbon studies. Mint cuttings were allowed to fix $C^{14}O_2$ for three hours in the light. One-third of the plants were harvested and the amount of activity in the oil determined. The other two-thirds were allowed to metabolize in a normal atmosphere and the oil that volatilized was collected in a toluene trap. This oil was found to contain one per cent of the activity of the oil originally present in the leaves. Chromatography of this oil showed that it was essentially the same as the oil in the plants. Metabolism of oil during the experiment was not measured and the value obtained simply indicated that a very significant amount of oil was lost continuously by evaporation.

Mugoflor

Mugoflor is a new aromatic chemical now being manufactured and offered by Verona Aromatics of Newark, N. J. This new synthetic possesses a lily-of-the-valley odor with a characteristic green note, but differs chemically from hydroxycitronellal. Since it's said to be stable in soaps and non-irritating, it can be specially recommended for use in compounds for perfuming soaps and cosmetic preparations. Its odor characteristics make it an excellent starting material for cyclamen, honeysuckle, lilac, linden flower, and similar perfume compounds.

Corday offers a spray perfume purse flacon, metered spray containing Toujour Moi, Fame, Zigane, Trapeze, Possession, and Jet perfumes. Refills are also available. Deluxe dusting powder is now being offered in a white plastic box with a colored lambswool puff.

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(*Continued from page 221*)

steroids in a product that may be used indiscriminately over long periods of time. The prolonged use of oral corticosteroids has been observed to be acnegenic. Although the route of administration and dosage is different in such instances, there is the possibility of provoking new lesions or aggravating existing lesions, if the rate of absorption of corticosteroid and amount delivered to the reactive areas is sufficient. In this regard, how much corticosteroid for how long a time, are primary considerations. There are also some types of acne in which the topical corticosteroids are not indicated.

Even to imply that most acne patients may be controlled with self-prescribed scrubbings and a peeling lotion is a bit of foolishness. Most patients with acne require the professional advice of a competent dermatologist and the use of a therapeutic regimen in which scrubbing and topical therapy constitute one part. Dietary restrictions may be very useful, as is the administration of erythema doses of U. V. light. In instances where infection is a problem, systemically administered antibiotics are indicated. But, above all, effective therapy requires providing the patient—especially the adolescent—*with a point of view*—a point of view that will motivate him to carry out the treatment regimen systematically. This is a most important aspect of effective therapy. Unfortunately, this is not accomplished, either by self-treatment with an over-the-counter product, or by the doctor who is too busy to sit down with his patient and discuss the nature of the problem and what it takes—on the part of the patient—to achieve good results.

Seborrheic Dermatitis

At this point it might be appropriate to shift our discussion to a consideration of a somewhat related problem in which corticosteroids are also therapeutically effective, that is seborrheic dermatitis.

The population with seborrheic dermatitis is large, and the problems range from those with mild dandruff of the scalp to those whose problem is more wide-spread, severe, and persistent enough to consult the physician. As in acne, we cannot offer a cure; we can offer only a measure of control. We are, to a large extent, working in the dark because we know little or nothing about origin and pathogenesis. Similarly, we are not sure how the therapeutic agent achieves its effect. This is so for the use of tars, phenol, sulfur, mercury, resorcin, sulfacetamide, and selenium.

The addition of antibacterial agents (other than sulfacetamide) is based on a theory that seborrheic dermatitis is an infection. I know of no good evidence to substantiate this.

The one real important addition to the therapeutic armamentarium of seborrheic dermatitis in the past few years is the topical corticosteroid. Creams, oint-

(*Continued on page 234*)

Industry's Books . . .

Official Methods of Analysis, *9th ed., 832 pp., distributed only by the Association of Official Agricultural Chemists, Box 540, Benjamin Franklin Station, Washington 4, D. C.,* **$17.50.**

This compilation is the primary source of methods of analysis used by the Food and Drug Administration, U. S. Department of Agriculture, and other federal and state law-enforcement agencies in the the United State and throughout the world. The methods are used in law enforcement work because the extensive checking they have undergone to qualify for adoption by the Association gives them a high degree of reliability for use in developing court evidence to prove violations of the law. They are also used by laboratories engaged in research on foods, drugs, cosmetics, chemicals, and agricultural commodities.

Cutaneous Manifestations of the Reticuloendothelial Granulomas, *edited by Samuel M. Bluefarb, B.S., M.D., 442 pp., Charles C. Thomas—Publisher, Springfield, Ill. (1960), cloth.*

This volume is the fourth in a series of monographs pertaining to the cutaneous manifestations of diseases of the reticuloendothelial system. Only in recent years has the importance of its integrity been appreciated and attempts made to classify logically its many functional and anatomical vagaries. In a broad sense, the reticuloendothelial system may be said to participate to a major degree in the control of phagocytosis, antibody formation, and metabolism. One can, therefore, readily understand the high morbidity accompanying even slight disturbances in its natural operation. Emphasis is placed on systemic functional deviations and their relationship to those dermatoses customarily referred to as the "cutaneous lipoidoses." The section on biosynthesis of cholesterol is all-inclusive and does not represent or favor the views of any individual investigator. This book, by eight contributors, will be read and prized by medical student and practitioners, by clinician and pathologist.

Nerve Endings in Normal and Pathologic Skin, (Contributions to the Anatomy of Sensation), *by R. K. Winkelmann, M.D., Ph.D., Section of Dermatology, Mayo Clinic, Rochester, Minn., 195 pp., illus., Charles C. Thomas—Publisher, Springfield, Ill. (1960), cloth,* **$7.50.**

This book represents an effort to record a complete pattern of nerve endings in the skin of man. A similar study has been done for the cat and several other vertebrates; when pertinent, reference is made to this previous work. The chief emphasis is on human skin obtained from formalin-fixed surgical specimens and stained by means of silver and methylene blue technics, some of which were developed for this work. Satisfactory samples from all representative regions of the body are included, except for the eyelid and nasal skin, of which only fragments were obtained for study. This is an atlas as well as a book. A large number of illustrations provide complete visual documentation of points discussed in the text. It also contains over 400 references to the world's literature.

The Cutaneous Manifestations of the Benign Inflammatory Reticuloses, *Edited by Samuel M. Bluefarb, B.S., M.D., Associate Professor of Dermatology, Northwestern University Medical School, 408 pp., Charles C. Thomas — Publisher, Springfield, Ill. (1960), cloth,* **$14.**

The five volumes that make up this series of monographs have been compiled by Samuel M. Bluefarb, M.D. They include the pertinent literature and discuss the cutaneous aspects of diseases of the reticuloendothelial system. Contents: Chapter I. Introduction: The Reticuloendothelial System; II. Part 1—Introduction, Part 2—Juvenile Xanthcgranuloma, Part 3—Reticulohistiocytoma; III. Lmphocytoma Cutis (Lymphadenosis Benigna Cutis); IV. Granuloma Faciale (Facial Granuloma with Eosinophilia); V. Infectious Mononucleosis, all written by Samuel M. Bluefarb, M.D.; and VI. Lymphogranuloma Venereum; VII. Cat Scratch Disease, both by Orlando Canizares, M.D.; and VIII. Histoplasmosis by D. S. Kushner, M.D.

Mental Drugs: Chemistry's Challenge to Phychotherapy, *by O. A. Battista, Sc. D., 155 pp., Chilton Company, Bood Div., Philadelphia (1960), cloth,* **$3.95.**

This book will shock many, enrage more than a few, and offer hope to millions. Dr. Batista provides an authoritative and unbiased record of the mounting importance of chemistry and chemicals in the world-wide battle against mankind's most terrifying and most costly scourge—mental illness. Out of the current furor and confusion, a new and promising frontier is arising in the battle against complex mental disorders. Intensified research is under way on a hundred fronts, aimed at getting more and better information in response to the provacative disorders. The chapters in this book cover: Chemistry—New Champion of Sick Minds; The Chemistry of Moods and Emotions; Diet and Mental Health; The Chemistry of Mental Retardation; Turning Insanity On and Off—Through Chemistry; The Chemistry of Schizophrenia; Nature's Chemicals in the Treatment of Mental Illness; The Man-Made Tranquilizers; The Man-Made Antidepressants or Psychic Energizers; Greatest Ally of Mental Drug Therapy: Early Detection and Treatment; and Glossary of Mental Health Terms.

Chromatographic and Electrophoretic Techniques, Vol. I Chromatography—Second Ed., *Edited by Ivor Smith, Ph.D., Lecturer in Chemistry and Biochemistry, Courtaud Institute, Middlesex Hospital, London, 617 pp., Interscience Publishers, Inc., (1960), cloth,* **$10.75.**

Although less than two years have elapsed since the first edition of this work appeared, chromatographic methods have penetrated into many more fields and with the same valuable results. This new material is included in the present enlarged edition. The pattern of the new chapters, each written by an author well-versed in the field, follows that of the first edition. New chapters are devoted to DNP and PTH aminoacids, iodoaminoacids, inorganics, plant Polyphenols, alkaloids, radioactive techniques, ion exchange papers, etc., and most of the chapters of the first edition have been rewritten or revised to bring them up to date.

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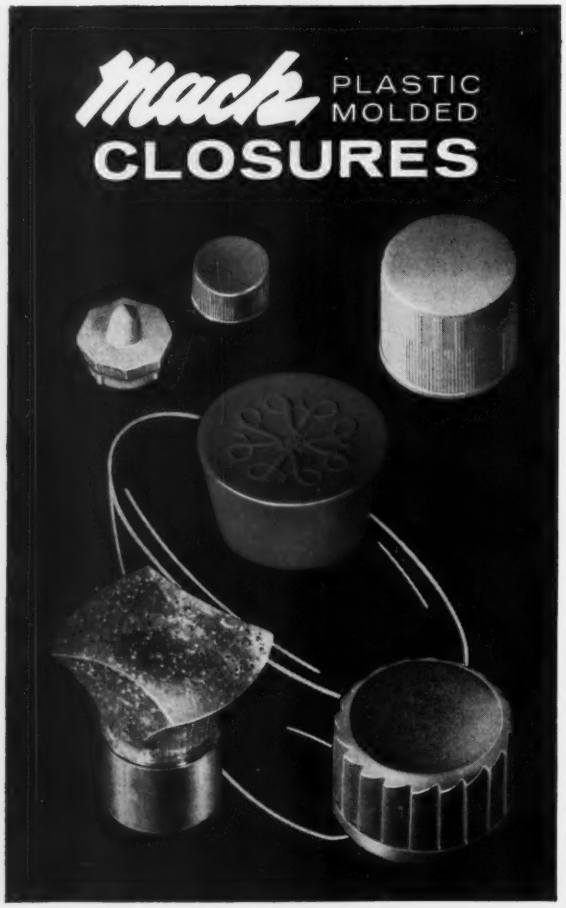

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(*Continued from page 230*)

ments, or lotions containing corticosteroids may be applied with good results to patches that are inflamed —on the scalp, face or trunk—and have, to some degree, supplanted the standard sulfur and salicylic acid medications used previously. In such conditions the corticosteroid preparation appears to be as effective as sulfur, salicylic acid, and/or tar preparations to which corticosteroids have been added.

Just as in acne preparations, it would be medically unjustified to incorporate corticosteroids into over-the-counter products for seborrheic dermatitis, since they may be used indiscriminately over a long period. Corticosteroids, even topically, should not be used unless a diagnosis has been established. In the presence of some infectious processes—bacterial or fungal—if employed without antibacterial or antifungal agents, corticosteroids might prove hazardous. With unrestricted use, even in relatively low concentrations, there is always the possibility of absorption of sufficient drug to give rise to systemic changes. Admittedly, the probability of such absorption from the use of a topical corticosteroid preparation is still very low, but all possibilities must be considered in an over-the-counter product usage.

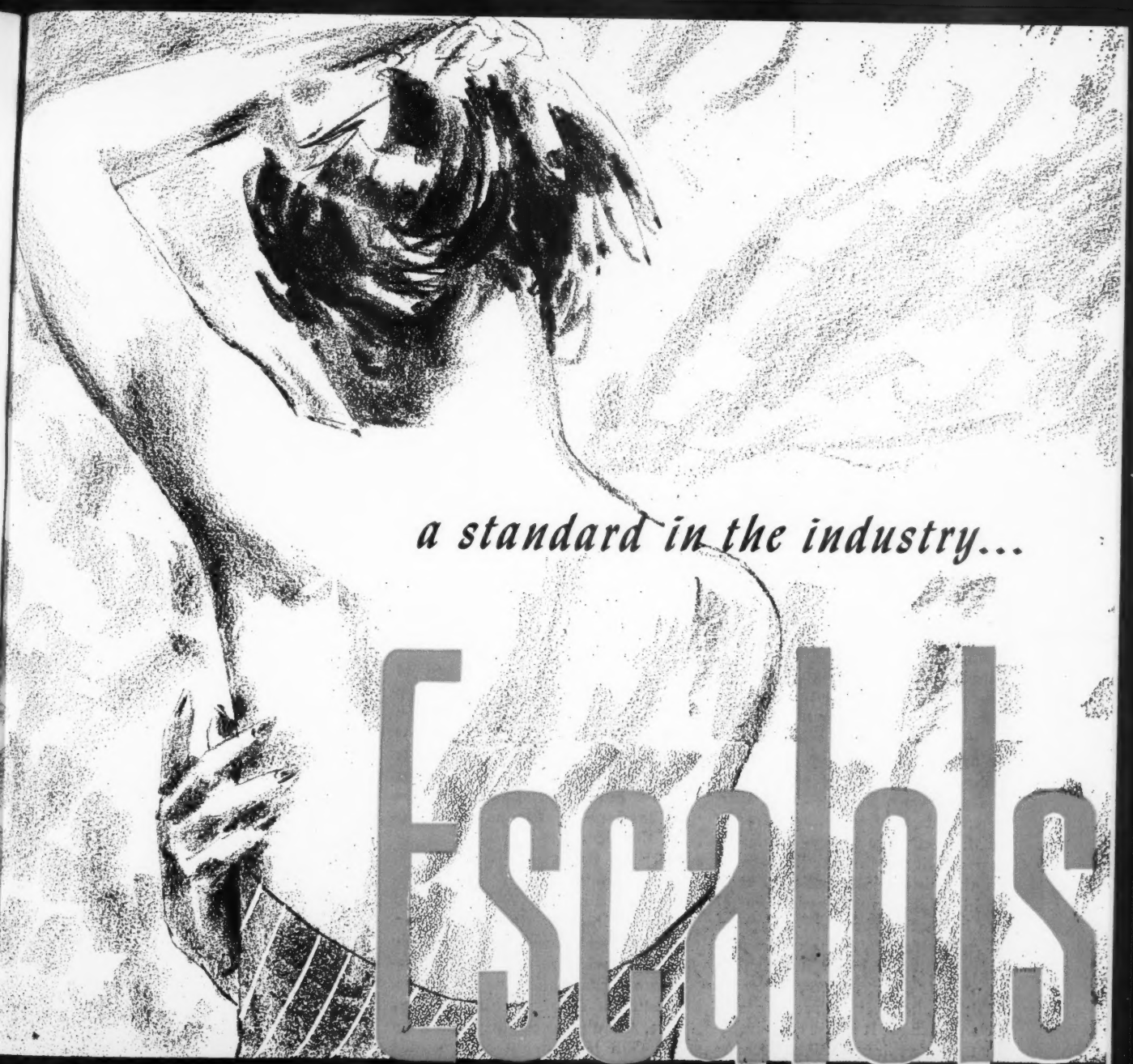
Fungous Diseases

We have observed that topical antifungal agents more effectively control the inflammatory lesions of tinea pedis and tinea cruris, if small amounts of corticosteroids are added to the formulations. In some instances where secondary bacterial infection is a threat, the addition of an antibiotic such as neomycin also has its benefits. It is well to recognize that there are medical indications for the use of both additives, and contraindications as well. If fissuring and maceration are not accompanied by inflammation, the use of topical corticosteroids would be unjustified. If the infecting agent is candida albicans, the use of neomycin might aggravate the problem. Hence, a shotgun preparation with a fungistatic agent, corticosteroid and antibiotic, would have some drawbacks.

I need not point out that antibiotics and corticosteroids are useful topical agents. Nevertheless, it is more important to appreciate the specific indications for employing such active agents therapeutically and the conditions of possible use which may give rise to undesirable consequences. With such knowledge as we now have, it would be unwise to incorporate these in proprietary formulas for acne, seborrheic dermatitis, and superficial fungous infections. Further study of these problems and acquisition of additional information, however, may give valid support for their incorporation into such preparations in the future.

The advent of griseofulvin was a real breakthrough in the treatment of fungous diseases. I am convinced that this is just the beginning, and research in this

(*Continued on page 242*)



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Skin Research

Antiperspirant Action

A decrease in axillary sweating following the use of aluminum salts has been observed by a number of investigators using various experimental technics such as starch-iodine and quantity of sweat absorbed by a measured amount of circulating hot air. Similar conclusions were drawn by Hermann *et al* using bromphenol-blue impregnated filter paper squares. Although this evidence demonstrates that aluminum salts decrease the amount of sweat on the surface of the skin, there is no agreement about how this is accomplished. A review of some of the past work indicates that antiperspirants may act either directly or indirectly on the sweat glands. A possibility of direct action is based on the histological studies of Ichibashi using formaldehyde. One of the indirect explanations is suggested by Rostenberg and Gonzales who reported that malonate ions topically applied decrease sweating by inhibiting the enzyme succinic acid dehydrogenase. It is also conceivable that antiperspirants might decrease sweating by direct pharmacological action such as an anticholinergic effect. However, the most widely accepted explanation was suggested by the observations of Shelley and Hurley and Hermann and Sulzberger that antisudorifics act indirectly by producing an inflammatory reaction with edema and expansion of the horny layer at the ductal orifice producing a narrowing of the pore thereby reducing the amount of sweat reaching the cutaneous surface.

Previous studies have substantiated the correlation between sweat gland activity and the Galvanic Skin Response (GSR). Measurement of the GSR thus provides a general method for studying the effects of certain drugs. The present study by D. J. Perry, G. E. Mount, and J. Maliner (*J. Invest. Dermatol.* 36: 7, 1961) was initiated to determine whether some topically applied compounds have a demonstrable effect on sweating as measured by the GSR Information obtained in this way might clarify the question of whether antiperspirants act directly or indirectly on sweat glands.

Aluminum chloride (25 and 33 per cent) in varying quantities up to 4.0 cc had no definitive effect on the GSR level. In previous reports the authors have demonstrated a lowering of the GSR level following oral or intramuscular administration of Banthine or atropine and a rise in this level after pilocarpine or mecholyl. Based upon these observations aluminum salts should produce a fall in GSR level if they had a local anhidrotic effect at the glandular level. Since there is ample clinical evidence that topical aluminum compounds reduce the amount of sweat reaching the surface, the absence of their effect on the GSR level might be construed as indicating that aluminum compounds reduce sweating by obstruction of sweat glands rather than acting at the glandular level. These present studies have not, however, precluded the chance that larger concentrations of aluminum salts might effect the GSR, a possibility that will be evaluated in future studies.

It is noteworthy that the axillary areas, containing both apocrine and eccrine glands, have been the sites of most previous investigations with antiperspirants. In the present studies the palms, which contain only eccrine glands, were tested. The question of what contribution the apocrine glands make might be clarified by similar GSR experiments in the axilla.

The present series included an evaluation of topically applied Banthine and Prantal on the GSR for several reasons. First, both compounds, when administered orally, have been shown to effectively reduce hyperhidrosis as demonstrated by Zupko and Prokop. This observation has been correlated with the effects of these two drugs on the GSR regardless of whether they are administered orally or parenterally. Secondly, Hirschmann reported a decrease in sweating following the topical application of 2 per cent and 5 per cent Prantal in a talc vehicle. However, the results of the present experiments using 5 per cent Prantal cream and 50-200 mgm. Banthine showed no inhibition of sweating indicated by a decrease in the GSR level. The question whether higher concentrations or other vehicles would produce different results by enhancing local absorption remains to be determined by additional studies.

Measuring Sweat

Diverse methods have been described for detecting sweat delivered to the surface of the skin. However, only a few of them are useful for visualizing the sweat delivery at the openings of the sweat ducts. In 1924, Jurgensen devised the counter-stain method to study sweating of the volar surface of the hand under microscope: the skin to be tested was painted with cedar oil which was then colored with a blue pencil, and sweating was made visible as pearl-like sweat droplets on the bluish background. Wada and Takagaki devised the iodine-starch reaction. In their method, sweat was visualized as black spots in a transparent layer of the mixture of corn-starch and castor oil coated on the skin

which was painted previously with iodine-alcohol solution. This method has come to be used widely in experimental and clinical investigations because of its simplicity and accuracy.

G. Tashiro, M. Wada, and M. Sakura: (*J. Invest. Dermatol.* 36: 3, 1961) have made a similar attempt at visualization with a color reaction of bromphenol blue. This reaction has already been used by Manuila in investigating the sweating in the human axilla, and by Hermann, Prose and Sulzberger in their printing method for quantitative estimation of sweating in small areas of the skin.

Dry bromphenol blue was dissolved in pure acetone in a 5 per cent solution, and then mixed with silicone (Dow Corning Corporation) with a viscosity of 5,000 centistokes at 25° C, in the ratio of 1:1 in volume. The mixture was stirred continuously in a mortar until the acetone was completely evaporated, and finally an orange-yellowish suspension was obtained. In this suspension the particles of bromphenol blue were found to be less than 3 microns in diameter. This indicator-suspension was kept in a desiccator when it was not used, but, it seems desirable to prepare it freshly before it is used.

The test area of the skin was wiped with cotton wool moistened with alcohol and was dried completely. Then the area was evenly painted with the indicator-suspension. When sweating occurred, bluish spots began to appear at the sites of the sweat pores and increased in size, as the sweating proceeded. When sweating was copious, coalescence of the spots was produced.

The method is advantageous in that sweat discharged from each sweat duct can be observed directly as a bluish spot or droplet through a transparent layer of the indicator-suspension. Further, the technic is simpler and less time-consuming than the iodine-starch method of Wada and Takagaki. The disadvantage is that the tested skin remains stained, making it difficult to repeat the procedure on the same test areas for the purpose of determining the duration of sweating.

Topical Hydrocortisone Safety

It is generally accepted that the external application of hydrocortisone is highly beneficial in the treatment of various chronic inflammatory and pruritic dermatoses.

Since the topical use of adrenal corticosteroids was introduced, two questions have arisen: 1) the question of the possibility of their percutaneous absorption, and 2) that of a risk of undesirable side effects resulting from prolonged usage, comparable with the effects at times produced by systemic administration of these compounds.

Regarding the first question there is experimental evidence that some percutaneous absorption of corticosteroids may occur following their topical application. In particular, Malkinson and Ferguson detected radioactivity in the urine following topical application of hydrocortisone-4-C^{14} and cortisone-4-C^{14} acetate. Under the conditions chosen, the peak of excretion of both compounds occurred at 48 hours and was followed by the excretion of smaller amounts for the next six days. Less than 1 per cent of the hydrocortison-4-C^{14} applied was excreted in the urine over a period of six days.

Scott and Kalz demonstrated the presence of C^{14} labelled hydrocortisone inside the skin and external application. By means of auto-radiographs the compound was detected in the epidermis, from where—upon transitory concentration in the basal cell layer—it assumedly moved into the cutis.

A number of investigations were reported in which laboratory tests were employed to explore the question of systemic effects of external corticosteroid application. Danto and Maddin did not observe any change in the number of circulating eosinophiles after the topical applications of cortisone. Similarly, Smith found no significant change in the circulating eosinophile count following the application of 150 mg. of hydrocortisone acetate to normal or clinically inflamed skin. In a similar investigation this author failed to note any changes in the urinary excretion of 17-ketosteroids and 17-hydroxycorticosteroids. Witten *et al.* studied the blood and urinary levels of 17, 21 dihydroxy-20-ketosteroids in response to external application of hydrocortisone for periods of three days without finding significant changes.

Gemzell *et al.* observed a reduction in the number of circulating eosinophiles and an increase in the 17-hydroxycorticosteroid blood levels following the inunction of 200 mg. of hydrocortisone incorporated in various vehicles—but both these changes were of low magnitude. Tschan and Adoni reported a decline of the circulating eosinophile count following the application of 2 ounces of an ointment containing 0.5 per cent prednisolone. This reduction was observed only when the count was above 100 prior to the inunction—and was significant in only 3 out of the 9 patients investigated.

All of these tests were carried on for only short periods of time (*i.e.* for approximately one to three days); the amounts of steroid employed were relatively small; and the skin areas contacted were in many instances unbroken and of minor extent.

It is for these reasons that the present assays were undertaken by R. Fleischmajer (*J. Invest. Dermatol.* 36: 11, 1961) in an endeavor to find out whether or not relatively large amounts of hydrocortisone applied to extensive areas of damaged skin may upon prolonged usage induce systemic effects and/or undesirable side effects, as would be detectable by close clinical observation and conventional laboratory tests.

Nineteen patients were selected of which 10 were females and 9 males. Their ages ranged from 5 to 60 years. The amount of hydrocortisone applied per subject ranged from 8,750 to 95,000 mg. The duration of treatment was from three to twenty months.

Clinical follow-up revealed no side effects which could be attributed to the hydrocortisone applications. Laboratory assays (performed at intervals), including circulating eosinophile counts, white blood cell differentiation, urinary 17-ketosteroid analyses, as well as quantitative assays of blood glucose and serum electrolytes did not show any distinct changes.

The results of this investigation strongly suggest that external hydrocortisone treatment does not produce any major systemic effects following the use of large amounts over prolonged periods of time.

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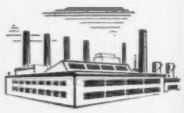
MANUFACTURING DEPARTMENT 	High and rapid solubility.	Compatible in multivitamin formulae.	Economical, less time and labor in compounding.	No solubilizer needed.	Make clear solutions of 30 mg. or higher per ml. of water.	No special techniques required. Relieve technical department problems.
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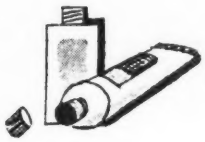

Advancing Therapy

Quick Sobering

An investigation of the use of thyroid hormone L-tri-iodothyromine by M. Goldberg, R. Hehir, and M. Hurowitz (*N. E. J. Med.* 263: 1336, 1960) in the management of acute alcoholism has shown this agent to have a prompt sobering-up action when given intravenously in a total dosage of 200 microgm Among 12 patients who received this treatment and were compared with 8 untreated, acutely intoxicated controls, the following results were obtained: the rate of blood alcohol decline averaged 15.0 mg. per 100 ml. per hour in the controls and 32.1 mg. per 100 ml. per hour in the treated patients; patients given the hormone were judged to be clinically sober and able to give a rational medical history within two hours after the injection; the odor of alcohol was undetectable on the breath two hours after treatment, although it persisted for six to ten hours in the untreated controls. Intravenous therapy appears to be a valuable adjunct in the treatment of acute alcoholism, particularly when such a patient is admitted to the hospital in a stuporous or semicomatose state secondary to severe intoxication and is unable to give a coherent medical history.

Hydroxamic Acid Tranquilizer

The pharmacology of hydroxamic acids has not been extensively studied. Epstein and Freeman have determined the approximate LD_{50} in mice for a number of aromatic and aliphatic hydroxamates and their effectiveness against sarin poisoning. Askey tested the toxicity of a number of other aromatic hydroxamates and found that most of them produced no overt symptoms at a dose level of 150 mg/kg. F. Bernheim and J. K. Stoops (*Proc. Soc. Exptl. Biol. Med.* 105: 542, 1960) prepared hydroxamic acids some of which were toxic, but others were well tolerated at relatively enormous doses despite the fact that these compounds are able to chelate cations such as iron, magnesium and calcium.

The hydroxamate of anthranilic acid injected intraperitoneally into rats in a dose of 1.0 m/g causes anesthesia lasting 10 hours or more. Recovery is apparently complete. One-half this dose causes tranquilization and suppression of the conditioned avoidance response. The compound protects mice against twice the lethal dose of strychnine. It merely prolongs the life of animals given metrazol or picrotoxin. A dose of 1.0 g/kg injected intravenously in a dog has no effect on heart rate, EKG or blood pressure and only minor effects on respiration. Equivalent amounts of a hydroxamates of salicylic and benzoic acids have none of the pharmacological effects.

Benzylthiazide Diuretic

The synthesis of chlorothiazide has stimulated the search for other substitution derivatives of the benzothiadiazine nucleus in the hope that these newer compounds might be less prone to induce potassium depletion. The newest compound belonging to this group is benzthiazide (3 - benzylthiomethyl - 6 - chloro - 7 - sulphamyl - 1,2,4, - benzothia - diazine-1,1-dioxide). The mode of action of chlorothiazide has been studied extensively (Bayliss *et al.*, 1958; Matheson and Morgan, 1958; Watson *et al.*, 1958), and a direct comparison with this drug provides the most satisfactory method of assessing the value of a new compound of this type.

The patients included in this series by C. W. H. Havard and D. H. N. Wood (*Brit. Med. J.* I, 1773, 1960) provide a stringent test for any diuretic. Only one patient with congestive cardiac failure had not received previous diuretic therapy, and in all patients the daily excretion of sodium during the control period was less than the dietary intake. This is largely due to the fact that since the advent of oral diuretics most patients with early congestive cardiac failure tend to be treated at home.

Benzthiazide by mouth is an effective diuretic. When compared in normal and edematous subjects a dose of 100 mg. produced a diuresis similar to that of 1 g. of chlorothiazide. The differences between the two drugs are in the effective dosage and in their action on bicarbonate excretion. Chlorothiazide increases the excretion of bicarbonate, whereas benzthiazide does not.

Benzthiazide causes a loss of chloride disproportionate to that of sodium. Bicarbonate excretion was unaltered, but potassium loss in the urine occurred just as readily. In patients with congestive cardiac failure the mean potassium excretion after benzthiazide was 54 mEq/day, compared with 59 mEq/day after chlorothiazide. Apart from this there were no toxic effects. The similar chemical structure of benzthiazide suggests that this drug may not be free from the occasional hazards of chlorothiazide (Nordqvist *et al.*, 1959), though the smaller dosage may be advantageous.

Antiviral Compound

"Virugon," formerly named "Flumidin," is being marketed in Europe for the prophylactic and therapeutic treatment of influenza and a number of other virus diseases and is the subject of a report in *Brit. Med. J.*, 1961, 1, 48.

The preparation contains N^1,N^5-anhydrobis (β-hydroxyethyl) bigu-

anide hydrochloride (ABOB) 100 mg. with atropine methonitrate (0.1 mg.) and scopolamine methonitrate (0.1 mg.).

This compound was discovered several years ago as a result of screening a series of biguanides for their effect in experimental influenza B. Melander reported that the effect of ABOB against experimental influenza in mice was marginal, but when combined with solanaceous alkaloids, which selectively reduce the secretions of the upper respiratory tract, it was found that the degree of pulmonary consolidation in certain strains was reduced. According to Melander, ABOB has a low level of toxicity. It has no antipyretic, analgesic, or spasmolytic properties, and no antihistamine or stimulant action on the central nervous system. It is readily absorbed from the alimentary tract and is rapidly excreted. No cumulative effect has been noted. Clinical trials were started in Sweden some seven years ago and have recently been reported. B. Sjoberg recorded the results of a double blind study with ABOB as a suppressant against influenza A[1] infection in Sweden in 1953-4, and with ABOB-X (i.e., ABOB with atropine and scopolamine methonitrate, "flumidin," virugon) as a suppressant and a prophylactic against Asian influenza in 1957. He claims that the differences between the groups treated with ABOB and ABOB-X are significant. They may be, but not many details are given of the method of assessment or of the results. With an adult dose of 100-200 mg. three times a day for suppression and prophylaxis very few side-reactions were encountered except for the occasional complaint of dryness of the mouth. B. Almberg and F. Stenkla have also expressed the view that these compounds exert a favorable effect on clinical influenza. B. Schersten reported that improvement was noticeable within two to three days of starting treatment with ABOB in 26 cases of herpes zoster in that pain quickly disappeared. The report is a short one. At a conference on occupational health in New York in October, 1960, several Swedish workers expressed the view that ABOB and ABOB-X were effective as prophylactics against influenza and other non-influenzal respiratory infections.

In Great Britain the results of a trial of virugon have been reported by the General Practitioner Research Group. The effect of the drug was studied in two groups of patients. Series A were 30 cases of chickenpox, mumps, herpes zoster, herpes labialis, and winter vomiting disease. Series B consisted of 56 patients suffering recurrent attacks of colds and recurring attacks of influenza. Patients in series A received virugon therapeutically and series B as a prophylactic. It is difficult to see from reading the report how these practitioners, with one exception, reached the conclusion that they were favorably impressed with the effect of virugon. The report contains few details, and the numbers —which are unstated—in each disease category appear to be small; while in the control groups of herpes zoster and herpes labialis there was only one case. Recently G. I. Watson has reported that virugon had no therapeutic effect against adenovirus type 3 infection in children, and no apparent effect against an influenza-like respiratory infection of unknown aetiology. In his two trials details are given of the numbers in each group, the dosage, and other forms of treatment, but the numbers again are small.

Thus it is hardly possible, on the basis of work published on this drug so far, to form a clear estimate of its therapeutic value, if indeed it has any.

Improving Drug Absorption

Because of their ability to decrease surface tension, surface-active agents supply one possible means of increasing absorption from the gastrointestinal tract following oral administration of drugs according to a review by T. H. Eickholt and W. F. White (*Drug Stand.* 28: 154, 1960).

Compounds including adrenocortical hormones, iron salts, some of the vitamins, neostigmine bromide, di-isopropyl fluorophosphate, sex hormones such as methyl testosterone and progesterone, and the digitalis glycosides are among the important drugs which are poorly absorbed from the gastrointestinal tract. Gastric juice has been shown to improve the absorption of vitamin B_{12}. Animal fat has been found to increase the absorption of vitamin A while vegetable oils have decreased its absorption. Vitamins D and K have also been more completely absorbed with the utilization of bile. Thiamine administered after fasting may be ninety per cent destroyed, whereas, if taken with food it may be two-thirds absorbed. The addition of sodium metaphosphate to the tetracycline compounds is a possible method of increasing their absorption from the gastrointestinal tract.

Many drugs and compounds have been absorbed better when administered with the surface-active agents. Spans, Tweens, polyethylene glycols, and Carbowax compounds have been studied by many investigators for possible toxic potentialities in order to validate or discredit their use internally.

Orally, the surfactants of large molecules have been found to be poorly absorbed, therefore, the acute oral toxicity of the polyethylene glycols has been found to be very low.

The toxicity of diotyl sodium sulfosuccinate in humans and in animals is low, however, some local gastrointestinal irritation has been observed with larger doses.

Polysorbate 80 given orally in humans, causes no toxic symptoms. Tween 80 increases the absorption of vitamin A as well as the absorption of fat.

Tween 20 orally has been found to increase the absorption of iron. High levels of iron have been found in the cecum, large intestine, the liver, and mesenteric lymph nodes. Better vitamin A absorption is obtained with Tween 20 and Tween 40. The mechanism of action of these agents is not understood but the site of action is thought to be in the intestine. Various authors have concluded that the surfactant possibly increases the permeability of intestinal epithelium or changes the iron, for example, into a more readily absorbable physical or chemical state.

The low order of magnitude of the toxicity of the surface-active agents would not hinder their use internally as agents to increase the absorption of poorly absorbed drugs from the gastrointestinal tract following oral administration.

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(*Continued from page 234*)

area will develop perhaps more potent antifungal agents that will be effective by topical application as well. When properly formulated, griseofulvin itself is effective topically both in tinea pedis and tinea corporis, but here again many questions regarding the percutaneous absorption and possible undesirable reactions with long-term use must be answered before incorporation into proprietaries can be justified.

A major problem in present-day high pressure promotion of proprietaries is the validity of the premarketing tests for effectiveness. This is as true for shampoos for dandruff as it is for fungicidal products.

I feel impelled to raise the question, because, in recent years, any number of proprietary products for seborrheic dermatitis incorporating relatively new chemical components have proved, after marketing, to be no more effective than either the detergent itself, or the time-honored anti-seborrheics such as sulfur, salicylic acid, or tar. It is also true of fungistatic agents, which, after much touting, have proved less effective than the standard undecyclenates. In accepting a new product, the physician will base his judgment on his own observations and on the patient's experience with the product prior to seeking medical advice. He will also be critical of a product if the premarketing appraisal has not been carried out properly. It is well to consider in any premarketing appraisal the need for: (1) a statistically significant number of samples; (2) a double-blind method of testing, including control formulas to limit bias; (3) well-trained observers who have dermatological experience; (4) an informative scoring technic for grading change in severity and for making repeated observations over a reasonable period of time; and (5) conducting tests during the period of the year when the problem is likely to be more severe.

The title of this presentation may seem somewhat misleading. Not really though, because the most significant thing about new trends in topical therapy is the more scientific and rational dermatologic approach to understanding disease processes and developing methods of correction. I have attempted to touch upon those aspects of topical therapy that seem to me to deserve the consideration of the developer and manufacturer of dermatological proprietaries. This approach, which I believe worthy of notice, should encompass an understanding of the normal biology of the skin, its aberrations in skin disease, and the rational methods that may be employed to treat the disorder. It provides the realization that single-treatment modalities are, in many skin diseases, far less effective than a combination of agents and therapeutic techniques; that, in the light of present knowledge, certain biologically active agents such as corticosteroids and antibiotics should not be incorporated into products that would be used indiscriminately over a long period of time; and that there is

a universe of worlds to conquor by fundamental research, including pharmacological research, from which will emerge new topical agents that will be useful to the patient and have the full confidence of the physician.

PHARMACEUTICAL PRODUCTS PARADE

(Continued from page 167)

methylenedisalicylate, presents this antibiotic in a more economic form, which may widen its application in combinations for the cemotherapy of amebiasis. This salt was developed by S. B. Penick & Company, and the first combination product was marketed by Chicago Pharmacal Company under the name of Anameba.

In the biological field, Merck Sharp & Dohme succeeded in producing a killed-virus polio vaccine of greater potency than those previously made. This vaccine, Purivax, is of uniform high potency and purity and is administered in doses of 0.5 instead of 1 cc. Immunity is obtained with Purivax within a shorter period of time and with less likelihood of allergic reactions. Multiple vaccines against tetanus, diphtheria, pertussis, and polio were marketed by Pitman-Moore. Both Parke, Davis and Pitman-Moore made available vaccines for adeno virus and influenza virus. Four manufacturers are currently supplying attenuated measles-virus vaccine for clinical evaluation.

The incidence of epilepsy remains high. In the United States 1,500,000 persons suffer from one or another form of epilepsy, and more than 30,000 patients are institutionalized. Recently introduced anticonvulsants offer a variation in therapy and may permit an increase in the degree of seizure control. The products introduced are Elipten (amino-glutethimide—Ciba), an analog of the hypnotic Doriden, and Zarontin (ethosuximide—Parke, Davis). Further studies are needed to clarify the exact positions these products may hold in the management of epilepsy.

To the group of appetite suppressants of the amphetamine type The Upjohn Company added Didrex (benzphetamine), which seems to be a suitable addition to the products available as symptomatic relief to the patient in his battle with excessive food intake. Several other combination products and preparations with a prolonged period of action were also marketed for this purpose.

Brief reference has already been made to the tranquilizer Librium (methaminodiazepoxide — Roche). This preparation, in resemblance to Dornwal (amphenidone—Maltbie) and Striatran (emylcamate—Merck Sharp & Dohme) differs chemically from the phenothiazine preparations so widely employed in therapy today. The claim has been made for Librium that it has a unique taming effect on the

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demons of anxiety and obsession in that it frees the patient from anxiety and tension without reducing mental alertness, dulling the senses, or decreasing perception. In a group of 593 patients who received Dornwal, sedation and drowsiness occurred only in 12 (1.8 per cent)—a low incidence as compared to other tranquilizers. Striatran, in addition to being a calmative, exerts a distinct muscle-relaxant effect. Timovan of Ayerst Laboratories is a derivative of phenothiazine and may find application especially in the disturbed adolescent and geriatric patient. Daily dose range is from 100 to 400 mg.

Various dosage forms and variations of hormones were prepared, their value depending on the ingenuity of the pharmaceutical development group of a manufacturer. Three new hormones deserve special mention: the anabolic hormones Dianabol (methandrostenolone—Ciba) and Adroyd (oxymetholone—Parke, Davis), and the hypoglycemic agent Glucagon (Lilly). The anabolic hormones increase nitrogen retention in the form of proteins to improve muscle and bone mass and to increase weight. These actions are particularly important in osteoporosis, in elderly debilitated patients, and in patients recovering from serious surgical or infectious illness. Recent studies suggest that a further extension of use can be expected for the anabolic hormones in other fields. Glucagon has been crystallized in pure form from animal pancreas by Eli Lilly and Company. Its main clinical indications are severe hypoglycemic reactions that may occur during insulin therapy of the labile diabetic, or during insulin shock.

The ever-present coughs and colds continue to induce manufacturers to market new products for their treatment. There were 31 new combination products, eight new dosage forms of previously existing preparations, and one innovation. The latter was ULO (chlorphedianol HCl.—Riker), available as a syrup for the specific treatment of coughs.

Dermatological therapy requiring antipruritics, emollients, fungicides, and many other agents, is receiving increasing attention from pharmaceutical manufacturers; eight new dosage forms and 30 new products were presented. Among the latter were the fungicides Pellar Ointment (Crookes-Barnes) and By-Na-Mid (butylphenamide—Cutter). The Schering Corporation synthesized a new steroid hormone, Diloderm (dichlorisone), which has a marked local antiinflammatory effect without producing a systemic action.

In the enzyme field, only drugs identical with, or variations of, previously available products were introduced. The same applies to eye preparations. Nothing spectacularly new can be reported for cardiovascular drugs.

The GI tract is still nervous and irritable. Hence there were 36 attempts to alkalize it (Riopan—Ayerst), to quiet its fast motion (Sorboquel—White, and Lomotil—Searle), or to hasten its sluggish ac-

tivity with laxatives, to provide it with bile, to aid its digestive action with new enzymes, to release excessive gas with silicones (Mylicon—Stuart) and to anesthetize the inflamed gastric mucosa (Oxaine—Wyeth).

In conclusion, we find that a number of products were marketed to aid the physician in his effort to diagnose disease conditions. Muscle relaxants have been combined with analgesics and cortisone. As for vitamins, there is simply no end to new formulations and variations.

The Source and Use of New Chemical Entities

An annual review of new products can only enumerate the most recent events; it does not interpret their broader meaning. I have therefore analyzed the new-product progress of the 20 largest pharmaceutical firms for a period of three years. This analysis provides some interesting data, as demonstrated in the following table.

PRODUCT DEVELOPMENT OF THE 20 LARGEST U. S. FIRMS

	Products marketed by				Total products	
	20 largest firms		Other firms*			
	Number	%	Number	%	Number	%
New chemical entities	89	58.5	63	41.5	152	15.3
Compounded products	182	27.7	476	72.3	658	66.0
Duplicate products	47	25.3	139	74.7	186	18.7
Totals	318	32.3	678	67.7	996	100.0
New dosage forms	176	56.6	135	43.4	311	——

*Including three firms owned abroad.

The first statistical observation to be made is that the 20 largest firms, which represented 12.2 per cent of the 156 pharmaceutical manufacturers nationally marketing new products during the three years of 1958 to 1960, supplied 89 of the 152 or 58.5 per cent of all new chemical entities and 32.2 per cent of all new products. According to the Associated Prescription Panel Service, the total product line of these firms received 64.4 per cent of all new prescriptions. Twenty-seven, or 29 per cent, of the 89 new chemical entities offered by the twenty largest firms came from abroad and were marketed in the U. S. partly by European-owned firms or by American manufacturers. Of the 63 new chemical entities marketed by the smaller firms, 25 were developed by foreign laboratories and 10 by U. S. manufacturers or individuals. Attention is also called to the fact that the 20 largest firms found it practical to market 176 or 56.6 per cent of all new dosage forms. Most of these dosage forms involved new chemical entities that these firms had previously marketed.

The breakdown by U. S. and foreign sources is as follows:

	U. S. development	Foreign development
New original products	30	20
Derivatives of known structures	16	7
New salts of old products	16	0
Totals	62	27

The next question arises: In what areas of re-

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search were the new chemical entities concentrated? If we judge merely by frequency, the following sequence can be established.

Diuretics	9	Analgesics & narcotics	4
Broad spectrum antibiotics	8	Antiinfectives including sulfonamides	4
Ataraxics	7	Eye preparations	4
Psychostimulants	5	Corticoid hormones	4
Dermatological preparations	5		

The balance of products is fairly evenly distributed among 32 other therapeutic classifications.

The development of new diuretic agents, with the exception of Geigy's Hygroton and Searle's Aldactone, was primarily a matter of following the leader —the introduction of Diuril by Merck Sharp & Dohme, which, together with HydroDiuril still dominates this important market. The question then arises: Does the deflection of a large amount of research time to the development of derivatives of this type pay? This question could be answered by analyzing, not only the research and promotion costs of such products with their current sales, but also the inroad of this type of product development on the total marketing resources of each firm; and this cannot be expressed in dollars and cents. If an original product is effective and produces few side reactions, the improvement that can be expected for analogs are only minor and the physician will continue to prescribe the original product with which he has become familiar.

Among the antibiotics marketed were such important products as Declomycin (Lederle), Ilosone and Vancocin of Eli Lilly and Company, which appreciably enhanced the effectiveness and scope of antibiotic therapy. Humatin (Parke, Davis), another antibiotic, was specifically designed for the treatment of amebiasis.

The introduction of Librium (Roche) and other nonphenothiazine ataraxics has started a battle royal with older tranquilizers. In this field, competition is extremely keen. The new products do not as yet seem to have extended the total use of tranquilizers—they have primarily brought about a shifting of positions.

Sale of monoamine oxidase inhibitors, successors to isoniazid, as psychostimulants has been somewhat disappointing. These products do not seem to have found the application that was expected in the treatment of depression. Recent reports suggest that they may find extended use in angina pectoris. (*Amer. J. Cario.* **6**:1103). Tofranil of Geigy, not an MAOI, has received wide publicity in medical journals for its use in the treatment of depression.

Dermatological practice benefited from the development of grisseofulvin, the first systemically effective fungicide, which has undergone several price reductions. The first systemic antipruritic therapy was accomplished with the phenothiazine derivative Temaril (Smith, Kline & French). Three analogs of cortisone brought about more specific therapy of dermatological inflammations.

The new narcotics and anesthetics can be regarded as a refinement in therapy. The same applies to two new sulfonamides. In relatively short succession we saw the introduction of the corticoids Aristocort (Lederle), Kenalog (Squibb), and Decadron (Merck Sharp & Dohme), followed by Schering with Deronil and by Ciba with Gammacorten. The latter firm also inaugurated a series of systemically active cough suppressants. The prospects of the cholesterol-reducing agent MER/29 have already been reviewed.

The Challenge of the Sixties

During the last 50 years, the practice of medicine has brought about tremendous changes in the age composition of the population. This change is largely due to a sharp decline in infant mortality. Whereas in 1900 the infant death rate in the United States was about 100 per 1000 live births, today it is in the mid-twenties, a rate slightly higher than the rate in some western European countries, in Australia, and New Zealand. Because of the decline of the death rate in infancy, more people live longer and more people are going to suffer from disease. While the general population doubled from 1900 on, the number of people over 65 years old quadrupled.

On the other hand, those who have bridged the age of 65 do not live very much longer than they used to. In 1900, life expectancy for a man who had attained the age of 65 was 12 years; in the ensuing six decades it has risen only to 14 or 15 years. There are indications that life expectancy has now reached a plateau that only revolutionary changes in medicine can be expected to change.

During the last 50 years we have also experienced a period of dramatic conquests in medical therapy unprecedented in history. From these conquests the medical profession and the pharmaceutical industry have derived great glory, applause and honor, and the industry has derived equally unprecedented profit. If we are wise enough to speculate about the future, we must face the probability that nothing of this sort is apt to be seen again. The era of the antibiotics and of new frontiers in vaccines—except for the treatment of the common cold—can be projected from now on only qualitatively, not quantitatively. The consequences of this "miracle" era are twofold: first, the saving of lives from infancy through the middle years, with continual increase in the proportion of the aged in the population; and second, because of the fanfare that has accompanied each conquest, enormously enlarged interest, knowledge, and heightening of the critical faculties of the general public.

As to the first of these consequences, the industry must now expect to supply an ever widening market of aging persons requiring primarily chronic disease therapies, and especially techniques and specifics to combat many inevitable deterioration-states that are not perhaps properly to be classed as pathological.

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From the socio-economic viewpoint, this means moving through the saving of life in a brief course of treatment, generally at a period when the patient is somewhere within his maximum earning potential, to a long-haul traffic in which needs must be supplied during the long period when earning power has dwindled, or is nonexistent.

The wise industrialist will adjust his sights to this new perspective, and possibly learn to operate on a basis of longer-term financial expectancy, with perhaps decreasing product obsolescence. The alternative, that the cost to the patient of maintenance therapies should continue to be in any way comparable to the cost of short-term therapy of infectious disease, is simply unrealistic, and could lead only to solutions highly distasteful not only to the industry but to the medical profession as well. What is required today is not so much innovation in industry and medical practices as a change in attitude, with the realization that the patient's needs must be served first. That is the challenge of the sixties.

WASHINGTON VIEWS

(*Continued from page 158*)

licensing of producers, generic name prescription drugs, patents, and more effective policing of drug advertising claims. With HEW now under Democratic control and having been re-elected, Kefauver is expected to clean up a few odds and ends, then make his valediction from the drug investigation via the issuance of reports supporting his legislative proposals.

The tocsin has been sounded for the drug and cosmetic industries! Their leaders recognize the threat of additional, unnecessary, and restrictive federal legislation as this year's No. 1 problem. These leaders of unjustly besmirched industries will oppose all but the public health. But, leave us cross that bridge when we come to it!

Attempting to simplify a report on the legislative problems facing the drug and cosmetic industries recalls Spearmint King Wrigley's reminder: "Anyone who remains calm in the midst of all this confusion simply does not understand the situation."

Kendall Group Clears FDA

Those familiar with FDA's administration of the law and its effective, fair, and common sense enforcement methods will not be surprised that the Kendall Group, following an intensive investigation into charges involving FDA employees and operations, concluded that FDA's essential functions are being performed; that decisions have not been made in defiance of the public interest; and that FDA personnel are more than ordinarily dedicated to the protection of the public health and economic well-being.

The Group's report also concluded that industry-FDA relationship can be stabilized at the level of

helpful cooperation. This should put an end to the unworthy tripe bandied about this past year reflecting unfairly on this conscientious agency and its dedicated and scientific-minded personnel. That the FDA staff grew reticent, nettled and non-plused by the unexpected and unjustified assault on its integrity is understandable. Now that the matter has been set straight, responsible industry representatives, sincere in their efforts to protect the public health, will find that a cooperative FDA-industry relationship based on mutual respect and confidence, continues. The Kendall report should go a long way toward preserving the "career" tradition of FDA's upper echelon.

Rx Promotion Regs Liberalized

A good example of FDA's common sense enforcement is its liberalization and clarification of the labeling disclosure requirements of its new regulations requiring manufacturers to furnish adequate information for the professional use of Rx drugs and devices (*Federal Register, January 14, 1961*). Following complaints from industry that it would be impracticable to effect full compliance with the provisions, effective January 8th, due to industry confusion and conflicting FDA opinions, a thirty-day extension was granted. In addition, the amended regulations permit until next January 1st the use of labels printed prior to January 8th, if the package or its inserts bear the information required by the regulation. Also, any carton packaged prior to January 8th may have its identifying lot or control number appear on either the label or the carton. The amended regulations extend to next January 1st the use of catalogs or price lists that lack full disclosure, if distributed to pharmacists or wholesale druggists, but not physicians.

The regulations were also amended to make clear that no package insert is required *solely* because the label bears the dosage information required by other sections of the FDA labeling regulations. The new Rx labeling regulations do not apply to advertising in medical and trade publications. Meanwhile, FDA is considering proposals by the American Medical Association, USP, and others to act as a clearing house for distributing pharmaceutical manufacturers' product brochures, which will furnish physicians with complete information on Rx drugs.

Landis Report on Regulatory Agencies

The Landis Report recommending presidential supervision over the enforcement programs and activities of the independent agencies will run afoul of stubborn opposition in Congress, if legislation implementing it should be introduced. It attacks a fundamental concept of our form of government and would disturb the relationship between Capitol Hill and the regulatory agencies, in addition to diminishing the independence of these quasi-judicial agencies.

The report emanated from a study made by James M. Landis, at the request of President Kennedy, who authorized its publication and named its author a special White House assistant, to oversee the independent agencies and implement the report.

The Landis recommendations involve some fine points of constitutional law. Under our complex system of administrative law, Congress delegates a considerable part of its authority to the independent agencies. Permitting presidential direction of that authority commingles the legislative and executive functions in contradiction of the delicately balanced doctrine of separation of powers in our constitutional law.

PRIVATE LABEL

(*Continued from page 159*)

flooded their private label suppliers with madcap ideas that often proved to be winners. Under this stimulation, very soon the private brand man began to contribute his own merchandising ideas and new products.

What products have come out of private label laboratories? We may not recall them all, but we can remember some important ones. Solid cologne in its present formulation was developed in a private label house, and was quickly followed by after shave sticks and deodorants. The liquid eyeliner first came from a private label manufacturer, and another manufacturer devised a medicated cake makeup. Pressed powder, deep-stain lipsticks, and liquid rouges were improved in this branch of the industry and, most recently, collaborative effort with a customer has resulted in a dry eye shadow preparation. This last provides an interesting example of quick product development. Once the idea was presented, little work was required to replace the red pigments in a dry rouge by the browns, blues, and greens needed for eye accent. In a large organization, the idea might well have been delayed because of higher priority projects, and could easily never have been pursued at all.

Because of his many-sided experience, the private brand manufacturer is a valuable adviser to those who are just entering the industry, and quite as often to established merchandisers. He has seen success and failure in the efforts of his customers, and knows what must be avoided. From experience, he is qualified to advise about packaging and can recommend sources of supply and designers, if necessary. He is certainly an expert on cost cutting, to the customer's benefit.

All in all, the private brand manufacturer has added a great deal to his original function. His lines and operations have a flexibility that permit him to handle special jobs or peak loads economically for

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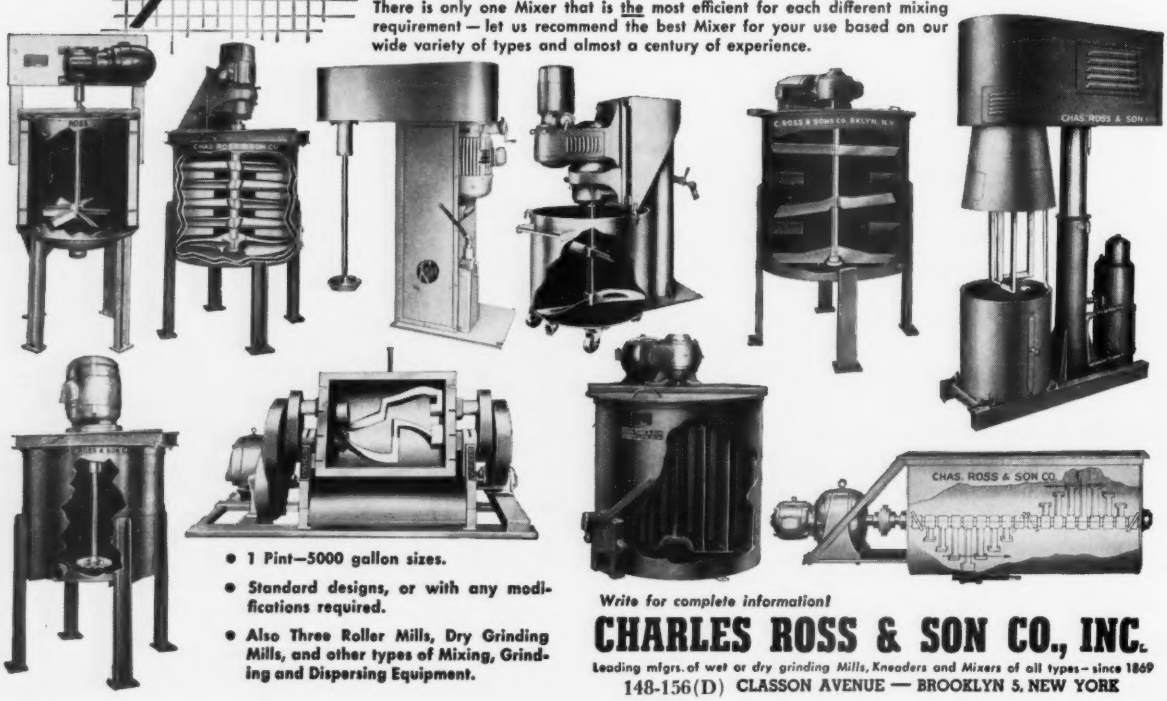

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TECHNIQUES OF PRODUCT DEVELOPMENT

(*Continued from page 165*)

change could make the price unrealistic. If the formulation contains one or more components whose price is considerably higher than that of others, these merit attention. There are two conventional approaches, substitution and reduction. If there were less expensive substitutes with just as desirable properties, these would probably have been included originally, which leaves only differences in degree available for discussion. Again, the questions become the willingness of the group to accept less than the originally desired level of characteristics, the affect on consumer appeal and selling price, and the time and cost involved in making the changes.

Theoretically, a firm with a new product that had been developed with due care and consideration from concept to pilot plant, would turn its attention to marketing considerations. Plans could be made for production, test markets, promotion, and distribution, and these could be carefully scheduled. The length of time involved from concept to wide distribution might appear too long, and susceptible to shortening. Since there are two phases, product development and market development, much time could be saved if the two were concurrent rather than sequential. The reasoning is flawless, but the scheme suffers from the poor quality of the available crystal balls. An operation which schedules hard and fast commitments for distribution and promotion facilities along with vaguer commitments of laboratory and pilot plant studies is asking for trouble, unless the schedule allows a large safety margin for the vaguer time periods. Unfortunately, the latter delays the telescoping aim of the concurrent progress and must be trimmed to the bone. A definite time commitment by a technical man is a prognostication based on the amount of time required for a known process, and may allow a time factor for an unknown, unexpected event. If the event does not take place, the schedule allows ample time and the technical prognosticator is an oracle. If the event does occur, the mails are too slow anyway.

COSMETIC REACTIONS

(*Continued from page 174*)

3. *Nail Polish.* Despite the fact that these chemicals are applied to the fingernails, they usually

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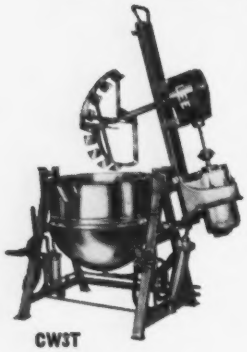

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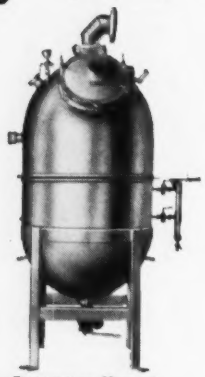
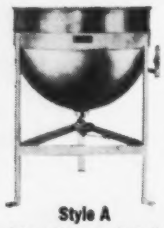


Pressure or Vacuum Reactors
to 500 gal.



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cause eruptions on the neck, face, particularly on eyelids, and not on the fingers. Nail polish is actually one of the frequent cosmetic causes of dermatitis of the eyelids. The offending chemical is most often a sulfonamide resin and is contained in the majority of nail polishes. There have also been instances of severe nail bed reaction to a nail polish undercoat, and these have been followed by subungual hemorrhage and loss of the nail proper. Fortunately, these reactions have become uncommon.

4. *Lipsticks.* An occasional cosmetic reaction due to lipstick is seen. Recently, the incidence was somewhat increased by the use of indelible dyes, but the resultant frequency of cutaneous reaction resulted in a rapid discontinuance of these products. The usual offender is a "bromo acid" eosin type of dye. However, it must be remembered that not all reactions on the lips are due to lipsticks. A classic example is that of the woman with severe swelling, scaling and cracking of the lips which, after months of study and exploration, was finally traced to her boy friend's moustache wax. Similar reactions on the lips have occurred as a result of exposure to products as exotic as bubble gum, and as prosaic as toothpaste.

5. *Deodorants and Antiperspirants.* These products usually contain aluminum derivatives, and often a small concentration of some antibacterial agent and a perfume. The aluminum derivative is the usual offender and in these instances the reaction is actually a low-grade primary irritation rather than an allergic sensitization. There have also been a few reports of granuloma formation following the use of antiperspirants containing zirconium salts.

6. *Face Creams and Lotions.* These preparations are usually innocuous, unless they contain special ingredients or "active" agents that are apt to produce some degree of cutaneous sensitization. No specific sensitizing agents stand out in this group, although from time to time some "wonder" cream or lotion is introduced with appropriate fanfare and, alas, the "wonder" ingredient is apt to cause sensitization rather than rejuvenation. The same generalization applies to powders, rouge, and foundation lotions.

7. *Eye Cosmetics.* Most members of this group, which includes eye shadow, mascara, and eyebrow pencil, are comparatively harmless, containing color pigments in various bases.

Diagnosis

The diagnosis is best made by careful evaluation of the individual instance.

The first and most important factor is a proper history. If a dermatitis has appeared following use of a new cosmetic, disappears after its discontinuance, and can be reproduced by re-use of the cosmetics, that's it! Additional diagnostic aids include the localization and clinical appearance of the eruption, which is usually a combination of redness (erythema), scal-

(*Continued on page 255*)

(*Continued from page 252*)

ing, and swelling (edema). If the reaction is a severe one, small "bumps" (papules) and "blisters" (vesicles) may also appear. In chronic cases, the skin becomes thickened (lichenified) and pigmented.

The diagnosis may be made with ease when a woman states that the painful swelling and cracking of her lips followed the use of a new lipstick, but if the same condition was caused by her boy friend's moustache wax, a great deal of detective work may have been necessary to track down the offending agent. So too, a dermatitis of the eyelids following the use of new eye makeup is easily diagnosed, but if the causative agent is nail polish it is less apparent to the examiner; and, if it is due to the rubber lining of an eyelash curler, it is even more difficult to detect. The clinician's diagnostic talents may be stretched to extreme lengths in some instances and additional diagnostic methods such as patch tests, usage studies, cosmetic diaries, and the like may be required in problem cases.

Patch Tests

At this point, a few words about patch tests[11] and their use in diagnosis is in order.

First, the usual and standard type of closed patch test is performed by applying the suspected material underneath a covering material. If air cannot enter, it is called an occlusive patch and is a very sensitive barometer of skin reactivity. A nonocclusive patch allows for the entrance of air and is a less reactive test. The cosmetic being so tested should, of course, be free of primary irritants, and the reaction is read within 48 hours.

Secondly, the open patch test more closely duplicates actual usage, in that the cosmetic is applied to the skin and allowed to remain on for 48 hours, taking some precaution to prevent its removal by rubbing, clothing, or other means. A more exact method would be the actual use of the cosmetic on the areas where the dermatitis had occurred in an attempt to reproduce the original eruption. This type of usage application is of far greater significance diagnostically, but cannot always be employed for obvious reasons.

Thirdly, the prophetic patch test (Schwartz-Peck)[12] consists of two closed patch applications of the cosmetic on a group of at least 200 volunteers. The first test remains on for two to five days and the second application is applied two weeks later and remains on for 24 hours. Schwartz recommends that this test be followed by a usage test of four weeks on the same 200 volunteers.

The fourth test is the so-called repeated insult patch test (Draize, Shelanski[12]) and consists of applications of the cosmetic to the same or different sites every other day for from 8 to 15 consecutive applications, on 100 volunteers. Two weeks after the last application, a final patch test is applied (only

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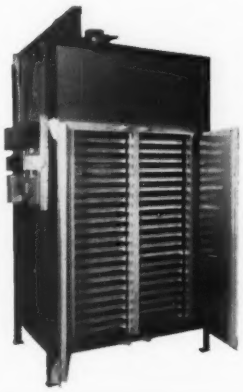

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if no previous reactions have occurred). This is a useful method of detecting weakly sensitising cosmetics but, from a practical standpoint, it is a difficult task to obtain the cooperation of the volunteer group.

In brief, the application of patch tests cannot be underestimated, although it should be recognized that they are not infallible. The test may be too rigid a criterion, or it may fail to pick up a culprit. They are not as useful as usage studies, but have a proper place in the evaluation of skin sensitizers when properly performed and statistically checked.

Treatment

The treatment is simple if the cause can be ascertained and eliminated. If a cosmetic allergy is suspected, it is sometimes necessary to have the patient stop all cosmetics for a week and then gradually reintroduce them at intervals of three to four days, in order to detect the guilty substance. If found, a substitute product may be employed or a break-down of the cosmetic may be necessary to reformulate a substitute acceptable to the user. This is not always possible.

Once a dermatitis has developed, local measures usually consist in the use of cold wet dressings such as boric acid or Burow's solution, bland creams and, if necessary, ointments containing steroid hormones. In those instances where the reaction is a severe one, the internal administration of antihistamines and especially of hormones (cortisone, ACTH) may be necessary. Desensitization is of little value and x-ray therapy is being used with less frequency.

Conclusion

In summation, we can predict that cosmetics will continue to be used in ever increasing amounts by both sexes. Although the great majority of cosmetics are harmless, new products should be thoroughly investigated before being released to the public. The evaluation, testing, and interpretation of safe cosmetics will rest in the hands of the dermatologist, who is ever more aware of his role in this phase of public health.

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COMING EVENTS . . . . .

FEBRUARY

13-15 **Pharmaceutical Manufacturers Assn.,** central regional meeting, Edgewater Beach Hotel, Chicago, Ill. (Dr. J. O'Neill Closs—P.M.A., 1411 K Street, Washington 5, D. C.)

15 **American Society of Perfumers,** open meeting, Advertising Club, 35th St. & Park Ave., N. Y. C. (A.S.P., 630 Fifth Ave., N. Y. C. 20.)

16 **Synthetic Organic Chemical Mfg. Assoc.,** luncheon meeting, Roosevelt Hotel, N. Y. C.

20-21 **Pharmaceutical Manufacturers Assn.,** western regional meeting, Ambassador Hotel, Los Angeles, Calif. (Dr. J. O'Neill Closs—see above.)

23-24 **National Beauty and Barber Manufacturers' Assn.** annual convention, Hotel Statler-Hilton, N. Y. C. (N.B. and B.M.A., National Press Bldg., Washington D. C.)

25 **American Institute of Chemical Engineers,** annual meeting and petrochemical exposition (to March 1), Municipal Auditorium, New Orleans, La. (A.I.C.E., 25 W. 45th St., N. Y. C.)

28 **Wayne State University College of Pharmacy and the Michigan Branch, American Pharmaceutical Assn.,** pharmacy seminar, McGregor Memorial Conference Center, Detroit, Mich. (Dr. Wm. L. Blackstein, College of Pharmacy, Wayne State Univ., Detroit, Mich.)

MARCH

1-3 **Pharmaceutical Manufacturers Assn.,** Medical Section, Ponte Verdra Club, Ponte Verdra, Fla. (Dr. Karl Bambach —see above.)

2 **Drug, Chemical and Allied Trades Assn.,** annual dinner and symposium, Waldorf-Astoria Hotel, N. Y. C. (Miss Helen L. Booth, D.C.A.T., 1 Liberty St., N. Y. C. 5)

2-3 **Federal Wholesale Druggists' Assn.,** mid-year meeting, Statler-Hilton Hotel, N. Y. C. (R. C. Schlotterer, F.W.D A , 2 Lexington Ave., N. Y. C. 10)

7 **Johns Hopkins University,** Mechanisms of Gastrointestinal Absorption, Sheration-East Hotel, Park Ave. at 51st St., N. Y. C.

8-10 **Pharmaceutical Manufacturers Assn.,** Medical Section, Ponte Vedra Club, Ponte Vedra Beach, Fla. (Dr. Karl Bambach—see above.)

9 **Pharmaceutical Advertising Club,** meeting Roosevelt Hotel, N. Y. C. (P.A.C., 489 Fifth Ave., N. Y. C.)

14 **Society of Cosmetic Chemists,** Chicago Chapter meeting, Henrici's Restaurant, Merchandise Mart, Chicago, Ill.

15 **American Society of Perfumers,** open meeting, Advertising Club, 35th St. & Park Ave., N. Y. C. (See above.)

15-18 **Pharmaceutical Wholesalers Assn.** convention, Las Vegas, Nev.

17 **St. John's University College of Pharmacy,** annual pharmacy congress, University Campus, Jamaica, L. I. (Annual Pharmacy Congress, St. John's University, Jamaica 32, N. Y.)

20-31 **Purdue Univ. Industrial Packaging Institute,** industrial packaging short course, Purdue Univ., Lafayette, Ind. (Mark E. Ocker, Memorial Center, P.U., Lafayette, Ind.)

21-30 **American Chemical Society,** spring meeting, St. Louis, Mo. (A. T. Winstead, A.C.S., 1155 Sixteenth St., N.W., Washington 6, D. C.)

31 **Packaging Institute and the National Paper Box Manufacturers Assn.,** symposium on set-up boxes, Sheraton Hotel, Philadelphia, Pa. (Chas. A. Feld, P.I., 342 Madison Ave., N. Y. C. 17)

APRIL

10-13 **American Management Assn. National Packaging Exposition and Conference,** Lakefront Exposition Hall,

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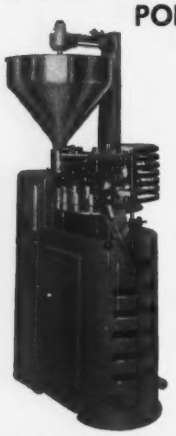

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APRIL *(Cont'd)*

Chicago, Ill. (A.M.A. Nat. Pack. Exposition, 1515 Broadway, N. Y. C. 36)

10-14 Federation of American Societies for Experimental Biology, 45th annual meeting, Atlantic City, N. J.

11 Society of Cosmetic Chemists, Chicago Chapter meeting, (See above).

13 Pharmaceutical Advertising Club, meeting, Roosevelt Hotel, N. Y. C. (See above.)

13 American Society of Perfumers, annual symposium, 2:00, Essex House, Central Park South, N. Y. C. (See above.)

20-21 Society of the Plastics Industry, western section conference, del Coronado Hotel, Coronado, Calif. (S.P.I., 250 Park Ave., N. Y. C. 17)

21 Parenteral Drug Assn., scientific meeting (all-day session) Edgewater Beach Hotel, Chicago, Ill. (P.D.A., 1420 Snyder Ave., Philadelphia 45, Penna.)

23-27 Society of American Bacteriologists, annual meeting, Morrisson Hotel, Chicago, Ill., preceded by a Symposium on Marine Microbiology (April 20-22) co-sponsored by the Office of Naval Research and the S.A.B. (J. C. McCaffrey, Ill. Dept. of Public Health, 1800 W. Fillmore St., Chicago 12, Ill.)

23-28 American Pharmaceutical Assn. annual meeting, Hotel Sherman, Chicago, Ill. (F. V. Porkorny, A.P.A., 2215 Constitution Ave., N.W., Washington 7, D. C.)

24-26 Animal Health Institute, annual meeting, Mayflower Hotel, Washington, D. C.

29 Toiletry Merchandisers Assn., to May 6, (Americana) Bal Harbour, Fla.

30 Pharmaceutical Manufacturer's Assn. annual meeting (to May 3), The Greenbrier, White Sulphur Springs, W. Va. (See above.)

MAY

1-3 Pharmaceutical Manufacturing Assn., annual meeting, The Greenbrier, White Sulphur Springs, W. Va. (See above.)

2-9 International Packaging Exhibition, Amsterdam, Holland (Verpakkingsbeurn, Tesselschadestraat 5, Amsterdam, Holland)

4-7 National Industrial Pharmaceutical Research annual conference, King's Gateway, Land O'Lakes, Wis.

9-11 Toilet Goods Assn., convention, and Scientific Section meeting (May 11), Waldorf-Astoria Hotel, N. Y. C. (Kathryn Fitzpatrick, T.G.A., 1270 Avenue of the Americas, N. Y. C. 20)

11 Pharmaceutical Conference, tenth annual, Rutgers Univ. College of Pharmacy, Newark, N. J.

11 Pharmaceutical Advertising Club, meeting, Roosevelt Hotel, N. Y. C. (See above.)

12 Society of Cosmetic Chemists, semi-annual meeting, Biltmore Hotel, N. Y. C. (S.C.C., 2 East 63 St., N. Y. C. 21)

14-17 Flavoring Extract Manufacturers Assn. annual meeting, Savoy-Hilton Hotel, N. Y. C. (John S. Hall, Hickery & Hall, 1051 First National Bank Bldg., Chicago 3, Ill.)

14-17 The Proprietary Assn., annual meeting, The Greenbrier, White Sulphur Springs, West Virginia (P.A., 810 Eighteenth St., N. W., Washington 6, D. C.)

15-17 Chemical Specialties Manufacturers Assn., annual meeting, Mayflower Hotel, Washington, D. C. (C.S.M.A., 50 E. 41st St., N. Y. C. 17)

17 American Society of Perfumers, closed meeting, Advertising Club, 35th St. & Park Ave., N. Y. C. (See above.)

22-25 American Society of Design Engineers, Design Engineering Show, Cobo Hall, Detroit, Mich. (Clapp & Poliak, Inc., 341 Madison Ave., N. Y. C. 17)

MAY *(Cont'd)*

22-26 **American Society of Tool and Manufacturing Engineers,** Engineering Conference and Tool Show, New York City Coliseum.

JUNE

4-7 **Annual National Industrial Pharmaceutical Research Conference,** King's Gateway, Land O' Lakes, Wisconsin, Extension Services in Pharmacy, University of Wisconsin (Richard S. Strommen, E.S.P., 301 Chemistry Bldg., University of Wisconsin, Madison, Wisc.)

5-9 **Society of Plastics Industry,** National Plastics Exposition and annual national conference, Coliseum and Hotel Commodore, N. Y. C. (S.P.I., 250 Park Ave., N. Y. C. 17)

9-17 **Achema, International Chemical Engineering Exposition and Congress,** including the annual meetings of the Dechema Society and the Isotopen-Studiengesellschaft, Frankfurt am Main, Germany (Chicago Section, A.C.S., 86 East Randolph St., Chicago 1, Ill.)

12-29 **Rochester Institute of Technology,** annual statistical quality control intensive courses for the chemical and processing industries, staff from American Society of Quality Control, Chemical Division, (industrial statistics and quality control, 12-21; design of experiments, 22-29; applications seminar, 20-21) Rochester, N. Y. (Harold M. Kentner, Director, Extended Services, Rochester Institute of Technology, Rochester 8, N. Y.)

13 **Society of Cosmetic Chemists,** Chicago Chapter meeting, (See above).

14 **Society of Plastics Engineers,** Plastics in Packaging, Quebec Section, Montreal, Quebec, Canada

15-16 **American Chemical Society,** National Colloid Symposium, Univ. of Rochester, Rochester, N. Y. (A.C.S., 1155 Sixteenth St., N. W. Washington 6, D. C.)

22-25 **American Therapeutic Society,** Essex House, N. Y. C.

23 **Parenteral Drug Assn.,** scientific meeting (afternoon and evening), Warwick Hotel, Philadelphia, Penna. (P.D.A. 1420 Snyder Ave., Philadelphia 45, Penna.)

25-30 **American Medical Assn.,** Exposition, New York City Coliseum, annual meeting, N. Y. C.

26-30 **Pharmaceutical Advertising Club,** meeting, N. Y. C. (See above.)

27-29 **Society for Investigative Dermatology,** N. Y. C.

AUGUST

10-16 **International Congress of Biochemistry,** Moscow, U.S.S.R. (N. W. Sissakian, Leninsky prospekt 33, Moscow, B-71, U.S.S.R.)

20-24 **American Veterinary Medical Assn.,** annual convention, Sheraton Cadillac Hotel, Detroit, Mich.

22-25 **International Pharmacological Meeting** (first), Stockholm, Sweden

SEPTEMBER

3-8 **American Chemical Society,** annual fall meeting, Chicago, Ill. (A.C.S., 155 Sixteenth St., N.W., Washington 6, D.C.)

4-8 **International Congress of Pharmaceutical Sciences,** Scientific Section, Pisa, Italy (Prof. Dott. A. E. Vitolo, General Secretary, Federation Internationale Pharmaceutique, Piazza Carrara, 10, Pisa, Italy)

5-8 **National Chemical Exposition,** concurrent with the fall national meeting of the **American Chemical Society,** The Chicago Ampitheater, Chicago, Ill. (Chicago Section, A.C.S., 86 Randolph St., Chicago 1, Ill.)

12 **Society of Cosmetic Chemists,** Chicago Chapter meeting, (See above.)

14 **Pharmaceutical Advertising Club,** meeting, Roosevelt Hotel, N. Y. C. (See above.)

14-17 **Drug, Chemical & Allied Trades Assn.,** annual meeting, Pocono Manor Inn, Pocono Manor, Pa.

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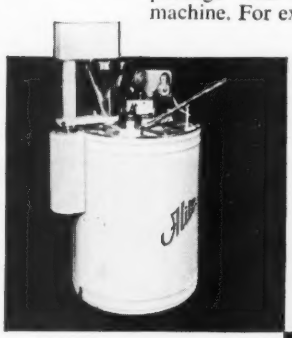

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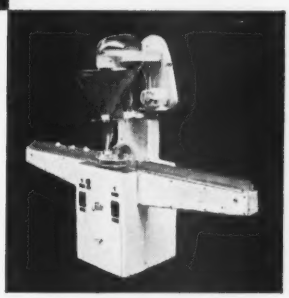

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SEPTEMBER *(Cont'd)*

20 American Society of Perfumers, closed meeting, Advertising Club, 35th St. & Park Ave., N. Y. C. (See above.)

24-27 Federal Wholesale Druggists Assn. annual meeting, The Greenbrier, White Sulphur Springs, W. Va. (R. C. Schlotterer, F.W.D.A., 2 Lexington Ave., N. Y. C. 10)

26-27 Society of Cosmetic Chemists seminar meeting, Barbizon Plaza (S.C.C., 2 East 63rd St., N. Y. C. 21)

29-30 American College of Apothecaries annual convention, Jack Tar Hotel, San Francisco, Calif.

OCTOBER

1-6 National Assn. of Retail Druggists' annual convention, Hotel Fountainbleau, Miami Beach, Fla. (N.A.R.D., 306 Kittridge Bldg., Denver, Colo.)

10 Society of Cosmetic Chemists, Chicago Chapter meeting, Henrici's Restaurant, Merchandise Mart, Chicago, Ill.

12 Pharmaceutical Advertising Club, meeting, Roosevelt Hotel, N. Y. C. (See above.)

14-19 National Wholesale Druggists' Assn., (Americana). Bal Harbour, Fla.

16-19 American Dental Assn., annual session, Philadelphia, Pa.

18 American Society of Perfumers, open meeting, Advertising Club, 35th St. & Park Ave., N. Y. C. (See above.)

18-20 Packaging Institute, annual national packaging forum, Biltmore Hotel, N. Y. C. (Chas. A. Leld, P.I., Inc., 342 Madison Ave., N. Y. C. 17)

NOVEMBER

1-3 Parenteral Drug Assn., annual convention, Statler-Hilton Hotel, N. Y. C. (P.D.A., 1420 Snyder Ave., Philadelphia 45, Penna.)

2-3 Society of Plastics Engineering Plastics in Packaging, North Texas Section, Sheraton-Dallas Hotel, Dallas, Texas

7-10 Packaging Machinery Manufacturers Institute Show, Cobo Hall, Detroit, Mich. (Hanson & Shea, Inc., One Gateway Center, Pittsburgh 22, Penna.)

14 Society of Cosmetic Chemists, Chicago Chapter, (See above.)

15 American Society of Perfumers, open meeting, Advertising Club, 35th St. & Park Ave., N. Y. C. (See above).

28 Society of Cosmetic Chemists, annual meeting and dinner dance, Biltmore Hotel, N. Y. C. (S.C.C., 2 East 63rd Street, N. Y. 21)

29 Toilet Goods Assn., Scientific Section meeting, Waldorf-Astoria Hotel, N.Y.C. (T.G.A., 1270 Avenue of the Americas, N.Y.C. 20)

DECEMBER

4-6 Chemical Specialties Manufacturers Assn., annual meeting, Roosevelt Hotel, N.Y.C. (C.S.M.A., 50 East 41st St, N.Y.C. 17)

14 Pharmaceutical Advertising Clubs, meeting, Roosevelt Hotel, N. Y. C. (See above.)

PATENT THOUGHTS AND TRENDS

(Continued from page 218)

Simply because we have labeled these as exceptions does not mean that they happen only rarely. In this connection, in a recent case, the ruling went against an Italian inventor in favor of an American inventor, even though the Italian could prove he

made the invention in Italy before the American made the invention in this country. Since the Italian did not disclose his invention in a patent or printed publication prior to the invention date of the American, the court ruled against the former.

The ruling in question has nothing to do with discrimination. Thus, if an American made an invention in Italy and the Italian made an invention in the U. S. A. and the facts were as in the case just noted, then the Italian would prevail.

The explanation for the courts' ruling as they do in these situations is found in the basic principles and fundamental philosophy of the Patent Law of the United States. The whole purpose of the Patent Law here is to grant a monopoly for a specified period to a person who makes an original invention and makes it available to the *American public*. If an invention is made in a foreign country and it is printed or patented, it is thereby given to the world and open to people of this country as well as to other countries. But, if a foreign discovery is not patented or printed in any form of publication, it might be known and used in remote places for ages and the people of this country, that is the U. S. A., would be unable to profit by it.

Recent Trademark Decisions

Poly Pitcher. A Federal District Court (Southern District, New York), recently ruled that Poly Pitcher is merely a descriptive of pitchers made of polyethylene.

Turino v. Tubino. The Patent Office Trademark Trial and Appeal Board (POTTAB) ruled that Turino, used for yarn made of synthetic fibers, is substantially similar to Tubino, used for thread and yarn of cotton, wool, linen, rayon, and mixtures thereof.

DCS v. DC. The POTTAB ruled that DCS, used for cutting oil, so resembles DC, used for lubricating oil, as to be likely to cause purchaser confusion.

Perma Line v. Permacel. The POTTAB ruled that Perma Line, used for thermoplastic road-marking compound, and Permacel, used for pressure-sensitive adhesive tapes, adhesive cements, heat sealing tapes, adhesive tape dispensers, tack cloth, abrasives, publications, steel wool pads, electrical insulation, and pre-paint cleaners, are sufficiently different to obviate any reasonable likelihood of purchaser confusion.

Tapemaster v. Tapemaster. The POTTAB ruled that Tapemaster, for gums, tapes, and dispensing machines, would not be likely to lead to confusion with Tapemaster, for tape dispensing and applying machines. The Board felt that, since the parties were not in competition with each other, since they make two distinctly different types of machines to handle tape, and since the products of the parties are sold through different channels of trade and under differ-

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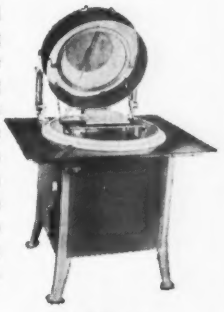

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ent circumstances and conditions to different classes of purchasers, no confusion would likely result. The Board also noted that, while one machine dispenses —in the broad sense of the term—protective tape, its applicability is not that of a dispenser but that of an applicator of tape.

SocietyDebs v. Stylish Debs. The POTTAB ruled that Society Debs, used for shoes, slippers, and boots, is not likely to cause purchaser confusion with Stylish Debs, for shoes. The Board felt that the terms Society and Stylish are common words of every day usage with well-understood meanings, and these words would not be likely to be confused by purchasers of shoes.

RECENT PATENTS

2,958,692—G. D. Searle—5-Carboxymethylmercapto-6-Aminouracils.

2,958,693—Burroughs-Wellcome—C-Substituted Piperazine Derivatives.

2,958,694—Paul Adriaan Jan Janssen—1-(Aroylalkyl)-4-(2'Pyridyl) Piperazines.

2,958,697—U. S. Vitamin & Pharmaceutical Corporation —Ethoxy Benzoate Esters.

2,958,699—Merck — Osmate Esters of 1-Carboalkoxy-Methyl - 2 - (Beta,Gamma - Dihydroxyisobutyl) - 2,4b - Dimethyl - 4 - Keto - 1,2,3,4,4a,4b,5,6,7,8,10;10a-Dodecahydrophenanthrene 7-Ketals.

2,958,700—Merck — 1-Carboalkoxymethyl-2-(Beta,Gamna - Dihydroxyisobutyl) - 2 - 4b - Dimethyl - 4 - Keto - 1,2,3,4,4a,4b,5,6,7,8,10,10a - Dodecahydrophenanthrene-7-Ketals.

2,959,517—Stauffer Chem. Co.—Bis (Trichloromethyl) Sulfone as a Biocide.

2,959,519—Monsanto — Fungicidal Composition Comprising a 2-Halo-4, 6-Bis (Amino)-S-Triazine.

2,959,520—Takeda Pharmaceutical Industries (Japan) —Stabilized Aqueous Solution of Vitamin B Complex Containing Cyanocobalamin and Thiocyanates.

2,959,584—Olin Mathieson — 4-Hydroxyprogesterone and Intermediate Therefor.

2,959,586—Smith, Kline & French Labs.—11, 18-Epoxy Steroid Compounds.

2,959,591—Sandoz Ltd. (Switzerland)—Reserpine-Like Esters of Pivalic Acid.

2,959,593—Sandoz Ltd. (Switzerland) — 3, 5-Dioxo-Pyrazolidines.

2,959,595—Monsanto—4, 4'-Thenylidene Bis Phenols.

2,959,601—Les Laboratories Francais de Chimiotherapie (France)—Steroidal Trans-Hexahydroterephthalate Esters.

2,959,602—Schering — Triesters of 9α-Fluoro-1, 4, 6-Pregnatriene-11β, 17α, 21-Triol-3, 20-Dione.

2,959,603—Schering — Triesters of 9α-Fluoro-4-Pregnene-11β, 17α, 21-Triol-3, 20-Dione.

2,960,434—Merck—15-Hydroxy-Progesterone.

2,960,435—Olin Mathieson—Synthesis of Steroids by Aspergillus Giganteus.

2,960,436—Olin Mathieson—Synthesis of Steroids by Diplodia Natalensis.
2,960,440—Max Jacobson—Anti-inflammatory and Analgesic Composition.
2,960,441—Warner-Lambert—Therapeutic Compositions of Salts of 3, 3-Pentamethylene-4-Hydroxybutyric Acid.
2,960,442—Schwartz Bio Research — Hair Dressing Method.
2,960,443—Breck—Temporary Hair Coloring Composition.
2,960,501—Upjohn — 2αMethyl-11β-Hydroxy-17α, 21-Epoxy-4-Pregnene-3, 20-Dione.
2,960,502—Upjohn — 6-Substituted Compounds of the Pregnane Series.
2,960,504—Ciba—1-Hydrazino, 4-Pyridyl Methylphthalazines.
2,960,505—Mozes J. Lewenstein—Morphine Derivative.
2,960,506—Ciba—New Esters of Reserpic Acid Alkyl Esters.
2,960,508—Miles Labs.—Certain 2-(1-Alkenyl)-Oxazolidines.
2,960,513—Olin Mathieson — Δ^1-Androstene-7α-OL-3, 17-Dione and Esters Thereof.
2,961,320—Gaxo Laboratories—Human Dietary Preparations.
2,961,374—Hans Lieb et al—Injectable Pharmaceutical Preparation.
2,961,375—Charles G. Shaw—Nontoxic Fungicidal Preparations.
2,961,377—U. S. Vitamin & Pharmaceutical Corporation—Oral Anti-Diabetic Compositions.
2,961,442—Abbot Labs. — β-Substituted-Ethyl Piperazines.
2,962,420—University of Illinois Foundation—Method of Inhibiting Perspiration and Compositions Therefor.
2,962,496—Geschickter Fund for Medical Research—N-Substituted-3-Azabicyclooctanes [3:3:0] and salts Thereof.
2,962,499—Endo Labs—Certain Esters of Tropine and Tropinium Salts.
2,962,500—Ciba—Alkyl-Piperidines.
2,962,501—Merck—1-Substituted Propyl Piperidines.
2,962,503—American Cyanamid—Nitropyrroles.
2,962,510—Schering A. G., — $\Delta^{1,4,6}$-Pregnatriene-17α-Ol-3, 20-Dione Esters.
2,962,511—Chattanooga Medicine Company—Benzenesulfonylhydrazones (O).
2,962,514—Abbott Labs. — p-Substituted Benezenesulfonyl Cyclo-Propane Intermediate.
2,962,519—Merck — Phosphates of 2, 3-Dimethoxy-5-Methyl Hydroquinones.
2,962,530—Cilag-Chemie Limited—Bis-Sulfonyl Ureas.
2,963,350—Harry Gold—Blood Sugar Test.
2,963,357—IBC Research Labs.—Fertility Potentiating Process.
2,963,401—Chas. Pfizer—Rimociden
2,963,402—Nysco Laboratories, Inc.—Sustained Release Medicament.
2,963,403—Upjohn—Defoamed Surface-Activated Mono-

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2,963,476—Ciba—2, 3-Dihydro-1, 4-Thiazine-3-Ones.

2,963,478—Smith, Kline & French Labs.—4, 7-Diamino-N-Aralkyl-2-Aryl-6-Pteridinecarboxamides.

2,963,479—Edward C. Taylor—2-Aryl-4, 7-Diamino-6-Cyanopteridines.

2,963,480—Edward C. Taylor et al.—6-Pteridinehydrazine and Amidrazone Derivatives.

2,963,481—Smith Kline & French Labs.—6-Pteridinecarboxylic Acid Esters.

2,963,482—Eli Lilly—Bis-Epoxypropyldiamines.

2,963,486—Ciba—Certain Bis (Alkylaminomethyl -Pyridines.

2,963,491—Societa Italiana Prodotti Schering—Oestra-1, 3, 5(10)-Triene-17β-O1-3-Y1-α-Oxyisobutyric acid.

2,963,492—Olin Mathieson — 12α-Halo-11-Oxygenated Progesterones.

2,963,493—Lasdon Foundation, Inc.—Androstan-16-O1-3-One Compounds.

2,963,495—Olin Mathieson—12α-Halo-3, 11-Oxygenated-17α-Hydroxy-20 Oxo Steroids of the Pregnane Series.

2,963,496—Olin Mathieson—9α-Halo-16-Dehydro Steroids of the Pregnane Series.

2,963,497—Upjohn—2, 6-Dimethyl Steroids of the Pregnane Series.

2,963,498—G. D. Searle—Dehydro Derivatives of 11-Oxygenated 17α-(Lower Alkanoyl)-Oxy-9α-Halopregnane-3, 20-Diones.

2,961,412—Liquefreeze Co. Inc.,—Method of Freezing Poultry.

2,961,418—Joachim Anschel—Relaxin Composition.

2,961,523—Olin Mathieson—Δ^1-Pregnene-9β, 11β-Oxido-6β, 12α-Diol-3, 20-Dione.

2,961,527—Ciba—18-O-Hetero Esters of Reserpine Acid Methyl Ester.

2,961,530—Sterling—3-Alkyl-4-Hydroxymethyl-4-Alkyloxazolidines.

2,961,537—Schering A. G., Berlin, Germany—Therapeutically valuable Carboxylic Acid Esters of 17-Alkyl-19-Nor-Testosterone.

2,961,539—G. D. Searle — 17α-Hydroxy-21-Fluoro-4-Pregnene-3, 11, 20-Trione.

2,961,540—Merck—9α-Fluoro-Δ^1-3, 20-Diketo-11, 21-Bis-Oxygenated-17-Hydroxy-Allopregnene 3-Semicarbazones.

2,961,541—Merck—16β-Alkyl Pregnenes And Intermediates Therefor.

2,961,542—Upjohn — 11-Oxygenated-6-Methyl-9α-Fluoro-Pregnadienes and Esters Thereof.

2,961,543—G. D. Searle—3, 17-Bixoxygenated Androst-4-En-9α-O1s.

2,961,544—Syntex S. A. Mexico—15-Hydroxy Steroids of the Pregnane Series.

2,961,552—Aktiebolaget Leo (Sweden)—Adrenocorticotropic Action-Retarding and Anti-Enzymatic Substances.

2,965,534—Monsanto—Inhibiting the Growth of Plant Viruses.

2,965,535 — Monsanto — Pentachlorobenzenesulfenyl

Chloride.

2,965,541—Upjohn—17α-Acetoxyprogesterone Compositions For Oral Use and Methods of Same.

2,965,542—Albert Castaigne—Pharmaceutical Product for Reducing the proportion of Cholesterol in the Blood.

2,965,543—Merck—Alcohol Detoxification of Pertussis Vaccines.

2,965,244—Am. Cyanamid—Tissue Culture Propagated Canine Distemper Virus and Vaccine Therefor.

2,965,546—Am. Cyanamid—Biological Conversion of 5a(11a)-Dehydrotetracyclines to Broad-Spectrum Antibiotics.

2,965,575—Monsanto—Antiseptic Detergent Compositions.

2,965,633—Parke, Davis & Co.—6-Diazo-5-Oxonorleucine.

2,965,634—Parke, Davis & Co.—Norleucine Derivatives and Process for Producing Same.

2,965,635—Parke, Davis & Co.—Norleucine Derivatives and Process for Producing Same.

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2,965,637—Parke, Davis & Co.—Norleucine Derivatives and Process for Producing Same.

2,965,640—Schering — 16-N-Substituted Steroids and Process for Manufacturing Same.

2,965,641—Searle—Derivatives of 1-(2-Aminoethyl)-5-Alkoxy-4-Pyridones.

2,965,643—Ciba—Derivatives of Pyrazolo (3, 4-d)Pyrimidines.

2,965,646—Hoffmann-La Roche—Pyridylmethyldibenzylamines.

2,965,648—Christian Wiegand et al Certain 1-Alkenyl Benzimidazoles.

2,965,654—G. D. Searle—11-Oxygenated-21-Fluoro-4-Pregnene-3, 20-Dione.

2,965,675—Merck—Aniline Compounds.

2,966,442—American Home Products Corporation—Antibiotic Compositions.

2,966,443—Am. Cyanamid—Trivalent Poliomyelitis Live Virus Vaccine.

2,966,444—Takeda Phar. Ind., Japan—Enzymatic Oxygenative Production of 11- or 19-Position Hydroxylated Steroids.

2,966,486—Am. Cyanamid—16α, 17α-Substituted Methylene Dioxy Ethers of Steroids of the Pregnane Series.

2,966,487—G. D. Searle—3-Aminoalkylaminobenzotriazine-1-Oxides.

2,966,488—William Shive et al.—Substituted Alkylaminopurines.

2,966,490—Merck — N-[β-(p-Aminophenyl) Ethyl]-4-Carboethoxypiperidine.

2,966,491—Merck — N-Para Substituted-Phenylethyl-4-Phenyl-4-Carbalkoxy Piperidines.

2,966,492—Merck—Substituted Piperidine Compounds.

2,966,493-4—Ciba—New Pyridine Compounds.

2,966,501—Syntex S.A. Mexico—4-Halo Derivatives of 2-Hydroxymethylene Δ⁴-Androsten-17β-OL-3-One and the Corresponding 19-Nor Compounds. ●

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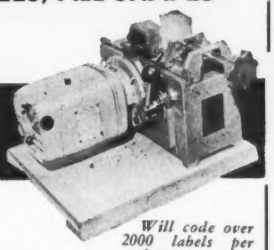

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COSMETIC CHEMIST: or pharmaceutist wanted for development research in cosmetic and allied products in moderate size, well-established company. Salary commensurate with experience. Furnish complete resume. Box F-2, Drug & Cosmetic Industry.

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